EXHIBIT 58 (part 1 of 2)

A
CBO
STUDY

HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY

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The Congress of the United States
Congressional Budget Office

NOTES

The numbers in the text and tables of this study may not add up to totals because of rounding.

Preface

In 1984, the Drug Price Competition and Patent Term Restoration Act (also known as the Hatch-Waxman Act) created an abbreviated approval process for generic prescription drugs and at the same time extended patent terms for innovator drugs. This Congressional Budget Office (CBO) study examines the extent to which competition from generic drugs has increased since the act. It also analyzes how that competition has affected the returns from developing a drug. The analysis was conducted at the request of the Chairman of the Senate Committee on the Budget.

Anna Cook of CBO's Natural Resources and Commerce Division wrote the study under the supervision of Jan Paul Acton and Elliot Schwartz. The analysis would not have been possible without data and information provided by the Food and Drug Administration (FDA), the Patent and Trademark Office (PTO), the Health Care Financing Administration, and Henry Grabowski of Duke University. A variety of industry experts provided information and insights, including Philip Chao and Donald Hare of the FDA, Karin Tyson of the PTO, Joel Hamilton of the General Accounting Office, David Reiffen of the Federal Trade Commission, Paul Wilson of IMS America, and Gary Persinger of the Pharmaceutical Research and Manufacturers of America (now of the National Pharmaceutical Council). Other outside reviewers included the following economics professors: Ernst Berndt and Scott Stern of MIT, Fiona Scott Morton of Stanford, David Salkever of Johns Hopkins, and F.M. Scherer of Harvard. Within CBO, John Peterson, Linda Bilheimer, Judith Wagner, Patrice Gordon, and Anne Cappabianca (now at Hoffman-La Roche) made extensive and valuable comments. Aaron Zeisler and Carl Muehlmann provided research assistance.

Christian Spoor edited the manuscript, and Melissa Burman proofread it. Angela McCollough typed the many drafts. Kathryn Quattrone prepared the study for publication, and Laurie Brown prepared the electronic version for CBO's World Wide Web site.

June E. O'Neill
Director

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Summary

The pharmaceutical market has become increasingly competitive since the early 1980s, in part because of the dramatic growth of the generic drug industry. In 1996, 43 percent of the prescription drugs sold in the United States (as measured in total countable units, such as tablets and capsules) were generic. Twelve years earlier, the figure was just 19 percent. Generic drugs cost less than their brand-name, or "innovator," counterparts. Thus, they have played an important role in holding down national spending on prescription drugs from what it would otherwise have been. Considering only sales through pharmacies, the Congressional Budget Office (CBO) estimates that by substituting generic for brand-name drugs, purchasers saved roughly $8 billion to $10 billion in 1994 (at retail prices).

Three factors are behind the dramatic rise in sales of generic drugs that has made those savings possible. First, the Drug Price Competition and Patent Term Restoration Act of 1984—commonly known as the Hatch-Waxman Act—made it easier and less costly for manufacturers to enter the market for generic, nonantibiotic drugs. Second, by 1980, most states had passed drug-product substitution laws that allowed pharmacists to dispense a generic drug even when the prescription called for a brand-name drug. And third, some government health programs, such as Medicaid, and many private health insurance plans have actively promoted such generic substitution.

Greater sales of generic drugs reduce the returns that pharmaceutical companies earn from developing brand-name drugs. The Hatch-Waxman Act aimed to limit that effect by extending the length of time that a new drug is under patent—and thus protected from generic competitors. Those extensions compensate for the fact that part of the time a drug is under patent it is being reviewed by the Food and Drug Administration (FDA) rather than being sold. The act tried to balance two competing objectives: encouraging competition from generic drugs while maintaining the incentive to invest in developing innovative drugs. It fell somewhat short of achieving that balance, however, in part because the act shortened the average time between the expiration of a brand-name drug's patent and the arrival of generic copies on the market (so-called generic entry) from more than three years to less than three months. More important, it also greatly increased the number of drugs that experience generic competition and, thus, contributed to an increase in the supply of generic drugs. In the end, the cost to producers of brand-name drugs from faster generic entry has roughly offset the benefit they receive from extended patent terms. Meanwhile, the greater competition from generic drugs has somewhat eroded their expected returns from research and development.

CBO estimates that those factors have lowered the average returns from marketing a new drug by roughly 12 percent (or $27 million in 1990 dollars). In this study, "returns from marketing a new drug" refers to the present discounted value of the total stream of future profits expected from an average brand-name drug. Previous studies estimate that those profits had an average present discounted value of $210 million to $230 million (in 1990 dollars) for drugs introduced in the early 1980s. Those returns are

valued at the date of market introduction, after subtracting production costs but not the costs of research and development. Also, because the drugs in those studies were not eligible for the patent-term extensions provided by the Hatch-Waxman Act, those estimates do not account for the benefits of the extensions now available under the act. Thus, those figures can be considered a minimum estimate of the returns from marketing. Only part of the estimated decline in returns can be attributed to the Hatch-Waxman Act; the other factors that have boosted sales of generic drugs have played a role as well.

This study relies on a variety of data to produce its estimates, including a data set that represents about 70 percent of prescription drug sales through retail pharmacies in the United States. The various sets of data all have strengths and weaknesses, which are discussed along with the estimates they generate. In general, the empirical estimates in this study are rough rather than precise measures. They help characterize the increase in competition in the pharmaceutical market and its effects on the profits of drug manufacturers and the prices paid for prescription drugs.

The Effects of Managed Care on the Pharmaceutical Market

At the same time that the Hatch-Waxman Act has helped increase the supply of generic drugs, changes in the demand for pharmaceuticals have affected the frequency with which generic and brand-name drugs are prescribed and the prices paid for them. Those changes in demand were brought on by newer forms of health care delivery and financing. In particular, because of competitive pressure in the health insurance market, more private-sector health plans have adopted managed care techniques in an effort to hold down overall health spending. The net effect of those techniques on spending for prescription drugs, however, is unclear.

On the one hand, many health plans (including traditional fee-for-service plans) hold down drug costs by "managing" their outpatient prescription drug benefits—either themselves or through organizations called pharmaceutical benefit management companies (PBMs). Those plans and PBMs use computer networks at pharmacies and electronic card systems for enrollees that allow pharmacists, before filling an enrollee's prescription, to consult a list (or formulary) of the plan's suggested drugs. Formularies typically encourage substituting brand-name drugs with generic versions, or sometimes with other, less expensive brand-name drugs. Savings result not only because of that substitution but also because many manufacturers of brand-name drugs offer discounts to health plans or PBMs in exchange for being included on their formulary. In addition, because they represent a large pool of customers, PBMs can negotiate with pharmacies over the retail prices charged for prescriptions. Since the late 1980s, those various techniques have been putting downward pressure on the prices that PBMs and health plans pay for prescription drugs sold through pharmacies.

On the other hand, health maintenance organizations (HMOs) and some other managed care plans frequently charge lower copayments for health care services—including physician visits and prescription drugs—than traditional fee-for-service plans do. Those lower copayments may lead to greater use of prescription drugs by beneficiaries. The treatment practices of HMOs may also favor more intensive use of prescription drugs, perhaps as an alternative to costlier forms of treatment. As a result, the increasing prevalence of managed care plans may have helped boost the quantity of prescription drugs sold in the United States.

For brand-name drugs still under patent (which do not yet have generic competitors), managed care techniques may have only a small effect on profits, assuming that greater use offsets the downward pressure on prices. For brand-name drugs whose patents have expired, however, profits are probably lower than they would have been without the generic substitution promoted in part by managed care plans and PBMs; that substitution has cut dramatically into the market share of those drugs. (CBO's calculation of the change in returns accounts for the full increase in generic market share since 1984, part of which is attributable to the rise in managed care techniques, but it does not measure managed care's effect on profitability through other variables, such as increases in prescription drug use and changes in pricing.)

Pricing and Competition in the Pharmaceutical Market

Competition in the pharmaceutical market takes three forms: among brand-name drugs that are therapeutically similar, between brand-name drugs and generic substitutes, and among generic versions of the same drug. Manufacturers of brand-name drugs compete for market share primarily through advertising and the quality of their products (including efficacy and side effects), as well as through pricing. Manufacturers of generic drugs increase their market share mainly by lowering prices. (In general, companies produce either generic or brand-name drugs, not both, although some generic manufacturers are subsidiaries of brand-name manufacturers.)

Competition Among Brand-Name Drugs

Patents do not grant complete monopoly power in the pharmaceutical industry. The reason is that companies can frequently discover and patent several different drugs that use the same basic mechanism to treat an illness. The first drug using the new mechanism to treat that illness—the breakthrough drug—usually has between one and six years on the market before a therapeutically similar patented drug (sometimes called a "me-too" drug) is introduced. Economic theory and various studies suggest that the presence of several therapeutically similar drugs limits manufacturers' ability to raise prices as much as would otherwise be the case. In addition, brand-name manufacturers are more likely to agree to give purchasers a discount if those purchasers have the option of switching to a generic or me-too competitor.

The factors that limit the number of similar but slightly differentiated brand-name drugs on the market are unclear. In some cases, perhaps, only a limited number of slightly different chemicals that target a given enzyme can be developed into drugs. Or, as one economist has suggested, the high cost of developing a drug may limit the number of similar brand-name drugs that are eventually brought to market. Companies will undertake such investment only if they believe the market is not already saturated or their drug has some quality advantage that could enable it to compete effectively and earn an adequate return. For that reason, competition among patented brand-name drugs probably results in companies' earning roughly a normal rate of return on their investment in research and development (R&D), on average.

Overall, the pharmaceutical market is not highly concentrated, but when that market is divided into narrowly defined therapeutic classes, it becomes quite concentrated. The top manufacturers of brand-name drugs, ranked by pharmaceutical sales, each account for no more than 7 percent of the entire market for prescription drugs (which totaled $60.7 billion in 1995 at manufacturer prices). Within each therapeutic class, however, higher levels of concentration appear. In 35 of the 66 therapeutic classes that CBO examined in this study, the top three innovator drugs together constituted at least 80 percent of retail pharmacy sales in their class.

Studies of the average prices paid by pharmacies and hospitals have shown that manufacturers of brand-name drugs do compete with each other through pricing. The markups they charge over the marginal cost of producing a drug are consistent with economic models of price competition in which entry by manufacturers is limited (such as by patents). Offering discounts to some buyers may also be an important dimension of price competition for brand-name drugs. But its extent is difficult to measure because of lack of data.

Discounts on Brand-Name Drugs

Different buyers pay different prices for brand-name prescription drugs. In theory, when companies are permitted to charge different types of purchasers different prices, those purchasers least sensitive to price will pay the most. In today's market for outpatient drugs, purchasers that have no insurance coverage for drugs, or third-party payers that do not use a formulary to manage their outpatient drug benefits, pay the highest prices for brand-name drugs.

Manufacturers offer discounts on brand-name drugs based not only on the volume purchased but also

on the buyer's ability to affect the drug's market share by using a formulary to systematically favor one brand-name drug over another for a large number of patients. Pharmacies themselves do not generally promote substitution between brand-name drugs, so they do not generally receive large discounts or rebates from manufacturers. Rather, it is the PBMs and insurers who manage benefits for drugs sold through pharmacies that promote brand-name substitution and receive discounts.

Such price discrimination, or discounting, may be an important mechanism for facilitating price competition in the pharmaceutical market. It rewards institutional purchasers that organize their patient base through formularies so as to encourage the use of less costly drugs. Prohibiting discounts, as some policymakers have called for, could decrease price competition.

Drug companies usually do not make their discounts public, but CBO was able to obtain limited information on the prices paid by different types of purchasers for prescription drugs. The prices that pharmacies pay can be seen as a proxy for the final price paid by customers who do not have a managed drug benefit or PBM to negotiate rebates from manufacturers. Based on the average invoice prices for top-selling drugs sold primarily to retail pharmacies, hospitals and clinics pay 9 percent less than retail pharmacies, on average, and HMOs pay 18 percent less. Federal facilities, such as veterans' hospitals, get an even more substantial discount—over 40 percent, on average, compared with the price paid by retail pharmacies. (Those comparisons are based only on invoice prices, so they do not account for rebates and other types of discounts that do not appear on invoices.)

Statistical analysis shows that manufacturers' discounts on brand-name drugs tend to be higher when more generic and me-too drugs are available. That analysis is based on the difference between the average price paid by pharmacies and the lowest price paid by any private purchaser in the United States (the best-price discount), as reported under the Medicaid drug rebate program. CBO found that the best-price discount for a brand-name drug was 10 to 14 percentage points greater when a generic version was available from four or more manufacturers. That analysis also showed that as the number of brand-name manufacturers in a therapeutic class increases from one to five, the best-price discount grows by 10 percentage points. Those statistical results imply that discounts are at least partly a response to competitive market conditions and may be a sign of greater price competition in some segments of the pharmaceutical market.

Competition Between Brand-Name and Generic Drugs

The Hatch-Waxman Act eliminated the duplicative tests that had been required for a generic drug to obtain approval from the FDA. (That change applied only to nonantibiotic drugs, since antibiotics already had an abbreviated approval process.) Before 1984, manufacturers of generic drugs were required to independently prove the safety and efficacy of their products. They were prohibited from using the unpublished test results of the original innovator drug, which were considered trade secrets of its manufacturer.[1] The Hatch-Waxman Act streamlined the process for approving generic drugs by requiring only that manufacturers demonstrate "bioequivalence" to an already-approved innovator drug. (Bioequivalence means that the active ingredient is absorbed at the same rate and to the same extent for the generic drug as for the innovator drug.) The tests necessary to prove bioequivalence are much less costly than those required to prove safety and efficacy.

By accelerating the approval process for a generic drug and also allowing its producer to begin clinical tests before the patent on the innovator drug had expired, the Hatch-Waxman Act reduced the average delay between patent expiration and generic entry from more than three years to less than three months for top-selling drugs. Even more important, the act increased the proportion of brand-name drugs that face generic competition once their patents expire. In 1983, only 35 percent of the top-selling drugs with expired patents (excluding antibiotics and drugs approved before 1962) had generic versions available. Today, nearly all do.

1. This study uses the terms "brand-name" and "innovator" interchangeably.

After a drug's patent expires, generic copies quickly gain a large share of its market. CBO examined 21 brand-name prescription drugs in its retail pharmacy data set that first saw generic competition between 1991 and 1993. Within their first full calendar year after patent expiration, those drugs lost an average of 44 percent of their market (as measured by the quantity of prescriptions sold through pharmacies) to generic drugs. And the generic versions cost an average of 25 percent less than the original brand-name drugs at retail prices. That rapid growth in generic market share after patent expiration is a substantial change from the situation before the 1984 Hatch-Waxman Act. In 1983, for example, generic market share averaged just 13 percent for nonantibiotic drugs.

Various studies have found that generic entry has little effect on the prices of brand-name drugs, which continue to increase faster than inflation. CBO's analysis of the average prices that manufacturers charge for drugs distributed to retail pharmacies is consistent with that result. However, CBO's analysis of discounting shows that certain purchasers other than retail pharmacies receive steeper discounts on brand-name drugs once generic alternatives are available. Taken together, those results imply that the impact of generic entry on brand-name prices may vary considerably among different types of purchasers.

Even if brand-name prices frequently do not respond to generic competition, such competition can effectively save money because price-sensitive buyers may switch to lower-priced generic drugs. CBO estimates that in 1994, purchasers saved a total of $8 billion to $10 billion on prescriptions at retail pharmacies by substituting generic drugs for their brand-name counterparts. (That estimate assumes that all of the generic prescriptions dispensed in 1994 would have been filled with a higher-priced brand-name drug if a generic drug was not available.)

Competition Among Generic Drugs

By making generic entry easier and less costly, the Hatch-Waxman Act helped increase the number of generic manufacturers producing the same drug. As the number of manufacturers rises, the average prescription price of a generic drug falls. CBO's analysis shows that when one to 10 firms are manufacturing and distributing generic forms of a particular drug, the generic retail price of that drug averages about 60 percent of the brand-name price. When more than 10 manufacturers have entered the market, the average generic prescription price falls to less than half of the brand-name price.

The Effects of the Hatch-Waxman Act on the Returns from Innovation

The patent provisions in the Hatch-Waxman Act have not completely protected drug companies' profits from the dramatic rise in generic competition since 1984. Manufacturers of brand-name drugs invest an average of about $200 million (in 1990 dollars) to bring a new drug to market, when the cost of capital and the cost of failures (investment in drugs that never make it to market) are included. Patent protection enables manufacturers to earn an adequate return on that investment. By itself, generic entry increases the rate at which sales erode after patent expiration, thus reducing the returns from marketing a new drug. Two studies have estimated that drugs introduced in the early 1980s earned returns that exceeded their capitalized costs of development by $22 million to $36 million, on average. (Those figures represent the present discounted value in 1990 dollars.) CBO concludes that since 1984, the expected returns from marketing a new drug have declined by about 12 percent, or $27 million in 1990 dollars. That decline has probably not made drug development unprofitable on average, but it may have made some specific projects unprofitable.

Changes to the Length of Patents for Brand-Name Drugs

Under the Hatch-Waxman Act, drugs that contain a new chemical entity never before approved by the FDA can qualify for an extension of their patent term. Those extensions, granted after the drug is approved, equal half of the time the drug spent in clinical testing (usually a total of six to eight years) plus all of the

time it spent having the FDA review its new drug application (usually about two years). Two key limitations apply. First, the extension cannot be longer than five years, and second, it cannot grant a total period of patent protection that exceeds 14 years after the drug is approved.

The 14-year limit is the main reason that Hatch-Waxman extensions now average about three years in length. Fifty-one drugs approved between 1992 and 1995 received an extension. Excluding the eight drugs that were subject to a transitional two-year cap (which applied to products already in testing when the act took effect), half of the drugs had their extensions limited by the 14-year cap.

Not all of the new drugs that are approved obtain an extension. Out of 101 drugs approved between 1992 and 1995, 38 did not apply for a Hatch-Waxman extension. Nineteen of those drugs had no patent to extend, and 15 others already had 14 years of patent protection left after obtaining FDA approval.

Besides patent-term extensions, the Hatch-Waxman Act contains other provisions that postpone generic competition. One key provision is the requirement that manufacturers wait five years after an innovator drug is approved before filing an application to sell a generic copy. That requirement benefits drugs that have no patent, or that have very little time left under patent, when they are approved. That exclusivity provision, together with the patent-term extensions, postpones generic entry by an average of 2.8 years for all drugs approved that contain a new chemical entity. Another exclusivity provision delays generic entry for three years when a new application is approved that requires clinical tests (such as for a new dosage form or over-the-counter version of an already-approved drug).

Ten years after the Hatch-Waxman Act, another piece of federal legislation—the Uruguay Round Agreements Act of 1994 (URAA)—further changed the patent terms of prescription drugs. That act altered the length of a patent for all types of inventions to 20 years from the date the application is filed rather than 17 years from the date the patent is granted. That change should have little effect on the average amount of time between market introduction and patent expiration for brand-name drugs patented after June 8, 1995 (most of which have yet to be introduced on the market). However, many products that were already under patent by that date have benefited from the URAA, since their manufacturers can choose between the 17-year and 20-year patent terms and still be eligible for a Hatch-Waxman extension.

The Change in Returns from Innovation

As noted earlier, the Hatch-Waxman Act greatly increased the probability that a generic copy would become available once the patent on a brand-name drug expired. It also contributed to a dramatic rise in generic market share. In addition, the act reduced the delay between patent expiration and generic entry, but that acceleration was roughly offset by patent-term extensions and exclusivity provisions that postpone generic entry.

CBO estimates that the increase in the size of the generic market since 1984—part of which is attributable to the act—has reduced the expected level of returns from marketing a brand-name drug by an average of $27 million in 1990 dollars. That amount is roughly 12 percent of the total discounted returns from selling a brand-name drug, which previous studies have estimated at $210 million to $230 million in 1990 dollars for drugs introduced in the early 1980s. (Those figures represent the present discounted value of the total stream of profits from those drugs discounted to the date of market introduction, deducting manufacturing costs but not R&D costs.) That 12 percent decline does not change significantly under reasonable variations in CBO's underlying assumptions.

Other factors besides the Hatch-Waxman Act have played a role in increasing the frequency of generic competition and the average size of generic market share. For example, changes in state laws have given pharmacists more leeway to substitute generic drugs for brand-name ones. And for reasons of cost, many purchasers have put increasing emphasis on generic substitution.

Total returns from selling a brand-name prescription drug vary significantly among different drugs. As noted above, the average cost of developing

such drugs, including failures, is around $200 million in 1990 dollars. But on average only three in 10 drugs earn that much in discounted returns (after deducting manufacturing, advertising, distribution, and other non-R&D-related costs). For most drugs, the returns from marketing do not exceed the average capitalized costs of development. As a result, for a company's average returns to exceed its average development costs, the company must discover and market a highly profitable drug from time to time.

For all drugs, on average, the increase in generic sales since 1984 has probably not reduced expected returns below the average capitalized costs of R&D. On the margin, however, it is possible that a few drugs that were barely profitable to develop before may no longer be so now.

CBO's calculation of the change in average returns since 1984 considers only increased generic entry and longer patent terms. It does not include many other changes that could either increase or decrease those returns—such as any rise in the volume of prescription drugs sold that might result as HMOs substitute drugs for more expensive forms of treatment and frequently charge lower copayments for prescription drugs and physicians' services. In addition, managed care plans and PBMs are putting downward pressure on the prices of brand-name drugs, which would tend to reduce the returns from selling them.

On the other side, returns could increase because drug companies' development projects may be improving as breakthroughs in the basic science of genetics are converted into ideas for new drugs. Moreover, foreign markets for prescription drugs should keep growing as the drug-approval process becomes streamlined in Europe, and many other countries continue to strengthen patent-protection rights.

Between 1983 and 1995, investment in R&D as a percentage of pharmaceutical sales by brand-name drug companies increased from 14.7 percent to 19.4 percent. Over the same period, U.S. pharmaceutical sales by those companies rose from $17 billion to $57 billion (in current dollars). Overall, then, the changes that have occurred since 1984 appear to be favoring investment in drug development.

Effects of Changing the Hatch-Waxman Act

Some representatives of the pharmaceutical industry have called for amending the Hatch-Waxman Act to lengthen patent-term extensions. However, doing that would not encourage innovation as much as accelerating the FDA approval process by the same amount would. The reason is that lengthening patent terms increases profits today for drugs whose patents are about to expire, but it does not have as great an impact on the incentive to invest in R&D—that is, on the expected average value of the profits from marketing a drug. CBO calculates that increasing the average patent term by one year would raise the expected value of those profits by about $12 million in 1990 dollars. Accelerating the FDA review period by one year would boost returns by much more—about $22 million in 1990 dollars. Thus, policies that speed up the FDA approval process without sacrificing the safety and efficacy of drugs are much more beneficial to both the pharmaceutical industry and consumers than is lengthening the patent-protection period.

Chapter One

Introduction

Competition in the pharmaceutical market has changed significantly. During the past decade, many health insurance companies have contracted out the management of their prescription drug benefits to specialized pharmaceutical benefit management companies (PBMs), and enrollment in managed care health plans has increased. In the previous decade, many states repealed antisubstitution laws that had prohibited pharmacists from dispensing generic drugs in place of brand-name ones, and changes in federal law sped up the approval process for generic drugs. All of those factors have contributed to a dramatic rise in sales of generic prescription drugs. Generic drugs contain the same active ingredient as a brand-name drug and enter the market after the patent on the brand-name drug has expired. Higher sales of generic drugs in turn have led to lower average prices for prescription drugs in general and a decline in returns from marketing new drugs.

The prices of brand-name prescription drugs are also facing downward pressure as many more purchasers try to negotiate discounts from manufacturers. In particular, PBMs and health maintenance organizations (HMOs) compile lists of suggested drugs (known as formularies) for their enrollees that encourage the use of generic drugs and less expensive brand-name drugs. The lure of being included on a large health plan's formulary allows those plans to leverage discounts on some brand-name drugs. According to the statistical analysis in this study, the discounts and rebates that some purchasers receive on brand-name drugs tend to be larger when more therapeutically similar brand-name drugs are available from different manufacturers and when generic copies are available. Such discounting may be an important source of price competition among brand-name drugs. However, assessing the amount of drugs sold at a significant discount is difficult, because sufficient data do not exist.

Market competition and federal policies have affected not only drug prices but also the incentives for companies to research and develop new drugs (in other words, to innovate). This study assesses the extent to which longer patents for innovative drugs—the result of 1984 legislation—have offset the effects of increased generic competition on the returns from marketing new drugs. The Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act) established provisions for extending patent terms for innovative drugs. At the same time, it reduced the testing requirements for approval of generic drugs, allowing them to enter the market—and thus cut into the sales of brand-name drugs—more quickly.

Many other changes have occurred on both the demand and supply side of the pharmaceutical market that affect the returns from innovation. This study examines many of those changes, but it does not attempt to explicitly measure their impact. On the supply side, recent breakthroughs in genetics and biomedical research have increased the technological opportunities for developing new drugs. On the demand side, the increase in HMO enrollment and the spread of managed care techniques to all forms of health insurance have made many purchasers more sensitive to drug prices and helped hold down those prices. At the

same time, under some forms of managed care, the demand for prescription drugs may grow. Because of those diverging trends of lower prices and higher demand, it is difficult to assess the net impact of the rise in managed care on profits in the pharmaceutical industry.

The Basis for Competition Among Drug Companies

Prescription drugs can be divided into two categories: innovator drugs and generic drugs. (See Box 1 for a glossary of various terms for prescription drugs.) Innovator drugs (which this study also refers to as brand-name drugs) generally have a patent on their chemical formulation or on their process of manufacture.[1] They have been approved by the Food and Drug Administration (FDA), after extensive clinical testing, under an original "new drug application" (NDA). Patented brand-name drugs that are therapeutically similar may exist, but each has a different chemical formulation. While they are still under patent protection, innovator drugs are called single-source drugs, because only the company that holds the patent produces them. After the patent has expired, generic copies of the exact chemical formulation usually become available. Then such drugs are referred to as multiple-source drugs.

Generic drugs obtain FDA approval under a shorter process than innovator drugs. They are required only to demonstrate "bioequivalence" to an innovator drug—in other words, to show that the active ingredient is released and absorbed at the same rate for the generic drug as for the corresponding innovator drug. Because they are copies rather than original formulations, generic drugs are not patentable.

Manufacturers of prescription drugs can be divided along similar lines: companies that primarily produce innovator drugs, and companies that focus on generic drugs. The two types of manufacturers compete very differently in the market. Producers of innovator drugs invest heavily in research and development (R&D), hoping to recoup that investment in profits from future sales while a drug is under patent and they have a monopoly on its manufacture. Producers of generic drugs do not need to duplicate the research effort of the innovator firm or invest nearly as much in getting FDA approval for their drugs. However, since those producers have neither patents nor a costly approval process to deter potential competitors, they quickly face competition from other companies pro-

Box 1.
Types of Prescription Drugs

innovator drug: a drug that receives a patent on its chemical formulation or manufacturing process, obtains approval from the Food and Drug Administration (FDA) after extensive testing, and is sold under a brand name.

brand-name drug: as used in this study, an innovator drug.

generic drug: a copy of an innovator drug, containing the same active ingredients, that the FDA judges to be comparable in terms of such factors as strength, quality, and therapeutic effectiveness. Generic copies may be sold after the patent on a brand-name drug has expired. Generic drugs are generally sold under their chemical name rather than under a brand name.

breakthrough drug: the first brand-name drug to use a particular therapeutic mechanism—that is, to use a particular method of treating a given disease.

me-too drug: a brand-name drug that uses the same therapeutic mechanism as a breakthrough drug and therefore competes with it directly.

single-source drug: a brand-name drug that is still under patent and thus is usually available from only one manufacturer.

multiple-source drug: a drug available in both brand-name and generic versions from a variety of manufacturers.

1. In a very small number of cases, generic drugs go by a brand name rather than the drug's chemical name. Those types of drugs are an exception and represent less than 2 percent of total retail pharmacy sales (based on tabulations of the Congressional Budget Office's data set on retail pharmacy sales). In this study, "brand-name drug" means an innovator drug.

ducing identical drugs. That intense competition forces generic manufacturers to charge much lower prices than the innovator firm—which, even after its patent expires, typically enjoys a market advantage based on its reputation for producing a high-quality product.

Although companies invest in research and development because they expect high returns from the future sales of their discoveries, those returns are considerably skewed. Some drugs have billion-dollar sales, whereas others bring in less than $25 million a year. For drug manufacturers to be successful, the present value of their future profits from the sale of new products (discounted to the date the products were introduced) must exceed the capitalized cost of their original R&D investment (capitalized to the date of market introduction), including investment in drugs that never make it to the market. Patents increase the rewards for innovation by giving companies a temporary monopoly over marketing their discoveries. Although that monopoly status rewards the company with high profits, consumers pay a higher price and get less output than would be the case under competition. But that temporary monopoly status is often necessary to provide sufficient incentives for drug companies to invent the new products that benefit consumers. Without patents, many new drugs could be easily and quickly duplicated by other manufacturers, preventing the innovator firm from obtaining enough reward to justify its investment.

Patents do not grant total monopoly power to companies in the pharmaceutical industry. In many cases, several chemicals can be developed that use the same basic mechanisms to treat a disease. Since a patent applies to a specific chemical or production process, different firms can end up patenting similar, competing drugs based on the same innovative principle. In addition, drug therapies often compete with nondrug therapies. Rather than having a pure monopoly, frequently drug companies produce slightly different products—leading to a form of imperfect competition that allows an innovator firm to earn higher profits than it could in a perfectly competitive market but less than it would with a pure monopoly.

Changes Made by the Hatch-Waxman Act

In passing the 1984 Hatch-Waxman Act, the Congress attempted to balance the interests of the generic drug industry against those of manufacturers of innovator drugs. That act contained two sets of changes. First, it eliminated the duplicative testing requirements necessary to obtain approval for a generic copy of a previously approved innovator drug. Specifically:

- It created an abbreviated approval process for generic copies of innovator drugs. A similar abbreviated process already existed under FDA regulations for generic copies of antibiotics and of innovator drugs approved before 1962.

- It allowed manufacturers of generic drugs to file an abbreviated new drug application and conduct clinical tests demonstrating bioequivalence with a brand-name drug before that drug's patent expires. As a result, the FDA can approve many of those applications immediately after patent expiration. That provision overturned a 1984 decision by the Court of Appeals for the Federal Circuit that clinical tests conducted by generic manufacturers before patent expiration constitute patent infringement.[2]

- It also established a process to handle patent disputes between generic manufacturers and innovator firms.

Those provisions helped to increase the availability of generic drugs following patent expiration.

Second, the act established patent-term extensions for innovator drugs. Because such drugs receive patents from the Patent and Trademark Office before they receive approval from the FDA, part of their time under patent is spent in the clinical trials necessary for

2. The case was *Roche Products, Inc. v. Bolar Pharmaceutical Company, Inc.* (733 F. 2d 858 Federal Circuit 1984). See also Alan D. Lourie, "Patent Term Restoration," *Journal of the Patent Office Society*, vol. 66, no. 10 (October 1984), pp. 526-550; and Donald O. Beers, *Generic and Innovator Drugs: A Guide to FDA Approval Requirements*, 11th ed. (Englewood Cliffs, N.J.: Aspen Publishers, 1995), pp. 4-75 to 4-77.

FDA approval. The patent extensions were intended to offset part of the patent term used up during the approval process.[3] Under the new procedures:

- Manufacturers of a newly approved innovator drug that contains an active ingredient never before approved by the FDA can apply for a patent-term extension that equals the sum of all the time spent in the NDA review process plus half of the time spent in the clinical testing phase. Two limitations exist. A patent-term extension cannot exceed five years, nor can it allow the period between product approval and patent expiration to exceed 14 years. The average length of patent-term extensions granted under this provision is three years.

- If an innovator drug is not protected by a patent, it may still benefit from certain exclusivity provisions that delay the approval or filing of an abbreviated new drug application in some cases.

By extending patents on brand-name drugs while making it easier for generic drugs to enter the market after patents expire, the Hatch-Waxman Act aimed to benefit consumers by increasing the supply of generic drugs while preserving drug companies' incentive to invest in research and development.[4]

Since the act took effect, pharmaceutical sales in the United States have risen dramatically. Between 1985 and 1995, sales of all prescription drugs by manufacturers grew faster than total health care spending. Valued at manufacturer prices, those sales increased from $21.6 billion to $60.7 billion—or from 5.7 percent to 6.9 percent of total health care expenditures in the United States.[5] Over the same period, spending on drug research and development rose even faster, growing from 15.1 percent to 19.4 percent of brand-name drug sales.[6] Although increased competition from generic drugs by itself reduces the returns from innovation, the rise in R&D spending indicates that, all factors taken together, a strong environment still exists for investing in drug development.

Data Used in This Analysis

This study contains a variety of empirical estimates that help to characterize competition in the pharmaceutical market and its impact on consumers and the returns from marketing new drugs. To produce those estimates, the study draws on several data sets. The largest is a set of data on retail sales by pharmacies; it represents about 70 percent of all sales of prescription drugs through pharmacies at retail prices and covers 66 therapeutic classes of drugs. Most of the estimates in Chapter 3—which include market shares and prices of brand-name and generic drugs and an attempt to approximate the savings obtained from generic substitution—rely on that data set. The statistical analysis of discounting in the pharmaceutical industry discussed in Chapter 3 also relies on that data set, as well as on price information made available through Medicaid's drug rebate program.

The calculation in Chapter 4 of changes in the returns from marketing innovator drugs relies on another set of data: figures on the U.S. sales of 67 drugs (introduced between 1980 and 1984) during their first eight to 12 years on the market. That calculation also uses the retail pharmacy data set to estimate the market share of generic drugs immediately after the patent expiration of a brand-name drug.

Each of those data sets has its own strengths and weaknesses, which are discussed along with the empirical results. A summary of the estimates made in this study, together with the methods and data sets that were used, appears in Appendix A.

3. See 35 U.S.C. 156(c), 98 Stat. 1598.

4. See, for example, the opening statement by Senator Orrin Hatch before the Senate Committee on Labor and Human Resources, June 28, 1984.

5. Data on total sales of prescription drugs, net of discounts and rebates and valued at the prices obtained by manufacturers, were provided by the Pharmaceutical Research and Manufacturers of America on April 28, 1997. If prescription drug sales had been valued at retail prices—the prices used for measuring national health expenditures—they would represent a higher percentage of such expenditures. Health care expenditures in the United States totaled $376.4 billion in 1985 and $878.8 billion in 1995; see Katherine R. Levit and others, "National Health Expenditures, 1995," *Health Care Financing Review*, vol. 18, no. 1 (Fall 1996), p. 179.

6. Pharmaceutical Research and Manufacturers of America, *1997 Industry Profile* (Washington, D.C.: PhRMA, March 1997), p. 57.

Chapter Two

The Effect of Managed Care on the Pharmaceutical Market

At the same time that the provisions of the Hatch-Waxman Act have affected the supply of generic drugs, changes in the demand for drugs—brought on by newer forms of health care delivery and financing—have influenced both the frequency with which generic and brand-name drugs are prescribed and the prices paid for them. Under competitive pressures, more health plans have adopted managed care techniques that help hold down overall health spending. The net effect of those techniques on prescription drug spending, however, is unclear.

The wider use of formularies has put downward pressure on the prices paid for brand-name drugs and has increased generic substitution. But use of prescription drugs may be higher in health maintenance organizations and some other types of managed care plans, because they tend to have more extensive coverage of physicians' services and sometimes of prescription drugs. In addition, managed care plans may sometimes favor the use of prescription drugs over other, more expensive, forms of medical treatment. As a result, the downward pressure on prices from the spread of managed care techniques may be offset by the more frequent use of prescription drugs.

The Rise of Managed Care

The shift of many people in the United States from conventional to managed care plans has been associated with an increasingly competitive market for health insurance, in which plans compete largely on the basis of price to maintain their market share. Managed care plans enjoy an advantage because they can generally charge lower prices than conventional insurance plans by negotiating better rates from doctors, hospitals, and other health care providers and by reducing the use of high-cost services. Because of that cost advantage, a large number of people have moved to managed care plans. According to the Bureau of Labor Statistics, the proportion of full-time workers with health insurance who were enrolled in such plans increased from around 26 percent in 1988 to 61 percent by 1995.[1] As a result, the cost of health care benefits for the private sector has grown more slowly in recent years (although it may now be on the rise again, with some health plans anticipating significant increases in 1999).[2]

In conventional health insurance plans—also known as indemnity, or fee-for-service, plans—enrollees can receive care from any physician or hospital they choose. Generally, they must pay for some initial

1. Those figures are for employees of medium to large firms; see Department of Labor, Bureau of Labor Statistics, "BLS Reports on Employee Benefits in Medium and Large Private Establishments, 1995" (press release, July 25, 1997, available at http://stats.bls.gov/special.requests/ocwc/oclt/ebs/ebnr0003.txt).

2. See Congressional Budget Office, *Trends in Health Care Spending by the Private Sector*, CBO Paper (April 1997); and Mercer/Foster Higgins, *National Survey of Employer-Sponsored Health Plans* (New York: Mercer/Foster Higgins, 1997).

amount of health care spending themselves (the deductible) and pay an additional amount (a copayment) of any costs beyond that. Conventional plans pay health care providers on a fee-for-service basis.

In managed care plans, by contrast, beneficiaries are encouraged to use a limited network of health care providers. The extent of that limitation, or the conditions under which a patient may choose a doctor or hospital outside the plan's network, can be used to broadly categorize the various types of managed care plans.[3]

- *Health Maintenance Organizations.* Enrollees in an HMO must generally receive all of their care from the HMO's physicians and from hospitals with which the HMO contracts; otherwise, the expense is not covered. The services they receive from those physicians are typically covered in full, apart from a flat dollar copayment for an office visit. (Copayments may also be required for such items as prescription drugs.) The plan's health care providers often bear some financial risk for the costs of the services they furnish or order on behalf of their patients.

- *Preferred Provider Organizations.* Enrollees in a PPO can receive services from any provider they choose, but typically they incur significantly lower deductibles and copayments if they use physicians and hospitals that are part of the PPO's network. The PPO pays providers in the network on a fee-for-service basis. Unlike in conventional insurance plans, however, those fees are subject to negotiation between providers and the plan.

- *Point-of-Service Plans.* POS plans are also known as HMO/PPO hybrids or open-ended HMOs. As in a PPO, enrollees can choose to receive services from providers who are not members of the plan's network as well as from those who are members. When enrollees use network providers, a POS plan functions much like an HMO. When they use other providers, by contrast, those providers are typically paid on a fee-for-service basis and enrollees are responsible for deductibles and copayments.

Many managed care plans transfer financial risk to physicians and other health care providers through the various financial arrangements they use to reimburse those providers. For example, some managed care plans use a form of capitation to reimburse physicians. In such cases, the physician (or group of physicians) is paid a fixed monthly amount per enrollee and is responsible for providing all primary care services —and in some instances, for paying for all medical services, including the use of specialists. When providers are at financial risk for the services they furnish or order for patients, they have a powerful incentive to provide less costly care. The net effect of that incentive on prescription drug use is not certain. But it could encourage providers to prescribe drugs in more cases rather than immediately selecting relatively expensive, procedure-oriented approaches.

An important trend in the spread of managed care techniques is that most types of health care plans —including conventional fee-for-service plans—have increasingly been "managing" their outpatient prescription drug benefits, frequently through pharmaceutical benefit management companies. Since 60 percent of prescription drugs are sold through pharmacies and other retail outlets, PBMs have become an important intermediary that helps limit costs for those drugs.

How PBMs Help Hold Down Drug Expenditures

Pharmaceutical benefit management companies exert downward pressure on the prices paid to both manufacturers and pharmacies. In return for channeling their patient base to particular pharmacies, they arrange to pay lower retail prices for drugs at those pharmacies. Similarly, PBMs are able to negotiate rebates from manufacturers of brand-name drugs based on their ability to steer their members toward a

3. The definitions below come from Congressional Budget Office, *Trends in Health Care Spending by the Private Sector*. That paper relied in part on a survey on employer benefits by KPMG Peat Marwick to develop those definitions; see KPMG Peat Marwick, *Health Benefits in 1995* (August 1995), p. 10. Many health insurance providers refer to their different insurance arrangements as products ("indemnity product," "point-of-service product," and the like). More than one product may be available from a particular provider to a company or individual enrollee. To be consistent with the earlier CBO paper, this study uses the term "plan" to refer to those products.

particular drug by using a formulary.[4] Those cost-saving methods are not limited to PBMs; some health insurers have set up similar operations to manage their own drug benefits. HMOs that have on-site pharmacies also apply formularies to promote the use of specific drugs and to negotiate rebates from drug manufacturers.

How Formularies and PBMs Operate

Typically, in a retail setting, formularies work as follows: a customer gives a prescription to a pharmacist to be filled and presents a membership card in a health insurance plan or PBM. The pharmacist then uses a computer network to check the plan's or PBM's list of preferred drugs as a guide in filling the prescription. Such lists frequently specify substituting a generic drug for a brand-name drug (something that has only been legal in most states since the late 1970s; see Box 2). In some cases, formularies also suggest substituting a less expensive brand-name drug for the one on the prescription. Promoting substitution between brand-name drugs is more difficult, however, since it requires the doctor's permission.

Using the same computer network, a PBM can track all prescription drug purchases by its members from pharmacies—providing it with a wealth of market data. PCS Health Systems, the largest PBM in the United States, in 1987 established the first electronic links with pharmacies that allowed two-way transmission of information and claims data.[5] PBMs never physically handle prescription drugs. Rather, they act as middlemen in a variety of transactions with health plans, pharmacies, and drug companies and thus insert themselves into the payment system (see Figure 1).

PBMs have found their niche as health insurance plans have expanded outpatient drug benefits. In 1972, just 20 percent of total retail drug spending was paid for by third parties (such as private-sector health plans or Medicaid). By 1995, that figure had tripled to 60 percent.[6] What share of those drug benefits is being managed by PBMs or health plans themselves is unclear, but it appears to be significant. According to IMS America, a company that supplies sales data on the pharmaceutical industry, 58.5 percent of retail pharmacies' revenues from drug sales in 1996 came from prescriptions that were at least partly paid for by

Box 2.
The Role of Changes in State Drug-Product Substitution Laws

The growth of generic substitution that has been fostered by the use of formularies would not have been possible without changes in state law. Through the early 1970s, it was illegal in many states for a pharmacist to dispense a generic drug when a prescription specified a brand-name one. By 1980, however, all but three states had drug-product substitution laws in effect that gave pharmacists more discretion. (By 1984, all states had such laws.)[1] Under those new laws, a pharmacist could dispense a generic drug even when a brand-name drug was specified, as long as the physician had not indicated otherwise on the prescription. By 1989, the dispensing of generic drugs on "brand-written" prescriptions rather than generically written prescriptions had become the chief source of generic drug sales through pharmacies.[2]

1. Alison Masson and Robert L. Steiner, *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws* (Federal Trade Commission, 1985), pp. 232-233, Table A4-1.

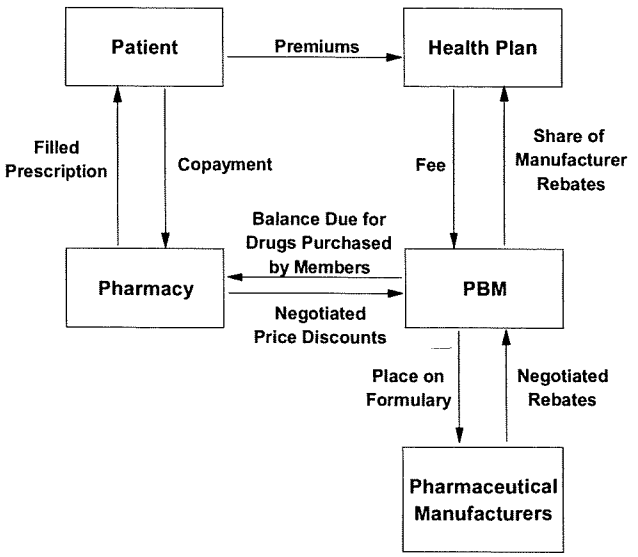
2. Richard E. Caves, Michael D. Whinston, and Mark A. Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry," *Brookings Papers on Economic Activity: Microeconomics* (1991), pp. 1-66.

4. See, for example, "PCS Rebates from Pfizer on Seven Products Totaled over $10 Million in First 21 Months of 1994-1998 Contract," *The Pink Sheet*, F-D-C Reports, June 10, 1996, p. 16.

5. Wilbur B. Pittinger, Senior Vice President for Health Management Services, "Placing PBMs in Context" (keynote address given at the roundtable conference of the Tufts Center for the Study of Drug Development, "PBMs: Reshaping the Pharmaceutical Distribution Network," October 24, 1996, available at http://www.pcshs.com/news/speeches/102496.html).

6. James S. Genuardi, Jean M. Stiller, and Gordon R. Trapnell, "Changing Prescription Drug Sector: New Expenditure Methodologies," *Health Care Financing Review* (Spring 1996), p. 192; and Katherine R. Levit and others, "National Health Expenditures, 1995," *Health Care Financing Review*, vol. 18, no. 1 (Fall 1996), p. 185.

Figure 1.
How PBMs Fit Into the Payment System for Prescription Drugs



SOURCE: Congressional Budget Office based in part on General Accounting Office, *Pharmacy Benefit Managers: Early Results on Ventures with Drug Manufacturers*, GAO/HEHS-96-45 (November 1995).

NOTE: PBMs = pharmaceutical benefit management companies.

third-party managed care drug coverage.[7] (That figure does not include cases in which patients paid for the entire prescription because they had not yet met their plan's deductible or the prescription price was less than their copayment, although in such cases the drug benefit may also be managed.) IMS America's definition of managed care third-party payment requires that customers presented an electronic card to the pharmacist indicating their membership in a health plan.[8]

Manufacturer Rebates and Pharmacy Prices

Much of the savings that PBMs achieve appear to come from the lower prices paid to pharmacies rather than from the rebates offered by drug manufacturers. The General Accounting Office studied three large health plans for federal employees that used both PBMs and mail-order pharmacies. The study found that 50 percent to 70 percent of the drop in the plans' spending on prescription drugs resulted from lower retail prescription prices (lower than what the plans would have paid at the pharmacy's usual and customary charge). Two percent to 21 percent of the savings resulted from manufacturer rebates that the PBMs shared with the health insurance plans.[9]

Generic Substitution

Another important way that PBMs lower drug costs is by promoting generic substitution, not just through formularies but also through their pricing contracts with pharmacies. In general, dispensing a generic drug is already slightly more profitable for a pharmacist than dispensing a brand-name drug.[10] PBMs' contracts sometimes provide financial incentives that make generic substitution even more profitable for pharmacists.

PBMs can also encourage generic substitution at the consumer level. In a conventional health plan, pre-

7. IMS America, "IMS Reports Major Regional Differences in Managed Care Growth" (press release, April 14, 1997, available at http://www.ims-america.com/communications/pr_regional.html).

8. Personal communication by Paul Wilson, Vice President of Statistical Services, IMS America, on March 1, 1998. If a customer had health insurance but applied for reimbursement later rather than presenting a card at the pharmacy, the transaction was considered a cash payment. Cash payments totaled 29.3 percent of pharmacies' drug revenues. Medicaid payments made up the remainder.

9. General Accounting Office, *Pharmacy Benefit Managers: FEHBP Plans Satisfied with Savings and Services, but Retail Pharmacies Have Concerns*, GAO/HEHS-97-47 (February 1997). In addition, Blue Cross found that in partnership with PCS Health Systems, it saved more on prescription drug expenditures through pharmacy discounts than through rebates from manufacturers (presentation by Alan Spielman, Vice President for Business Services, Blue Cross and Blue Shield Association, at the National Health Policy Forum "Purchasing as a Cost-Containment Tool: A Look at Pharmacy Benefit Management," Washington, D.C., May 12, 1995).

10. For most multiple-source drugs, the markup over the wholesale cost is higher (on an absolute dollar basis) for generic drugs than for brand-name drugs. In addition, because their wholesale cost is lower, the cost of having money tied up in stocks of generic drugs is lower. According to a recent study, for a prescription of 100 pills, the average retail markup on a generic prescription was about $13, compared with $10 on a brand-name prescription; see Henry Grabowski and John Vernon, "Longer Patents for Increased Generic Competition in the U.S.: The Hatch-Waxman Act After One Decade," *PharmacoEconomics* (1996), p. 116, Table IV.

scription drug coverage reduces the gap between the prices of brand-name and generic drugs as seen by the consumer. For example, if an innovator drug costs $40, its generic equivalent costs $20, and a health plan has a 20 percent copayment, then the consumer's price comparison is between $8 for the brand-name drug and $4 for the generic drug (after any deductible has been met). Because that price difference is small, the consumer may believe that the brand-name drug is worth an extra $4 and may prefer to have it dispensed. Many PBMs and health plans that manage their own drug benefits try to widen that price gap by charging a higher copayment for nonformulary drugs, such as brand-name drugs chosen over generic substitutes.[11]

Some researchers have found that even a small difference in the copayment can encourage generic substitution. One study determined that HMOs with a copayment difference of at least $2 between brand-name and generic drugs had as high a rate of generic substitution as HMOs that explicitly required such substitution.[12]

Industry Changes

Some analysts question whether the savings that PBMs produce will be adversely affected by recent changes in the industry. Several of the largest PBMs have been acquired by pharmaceutical manufacturers. PCS was bought by Eli Lilly in 1994 for $4 billion; Medco (both a PBM and a mail-order pharmacy) was acquired by Merck in 1993 for $6.6 billion; and Diversified Pharmaceutical Services was purchased by SmithKline Beecham in 1994 for $2.3 billion.[13] With acquisition, will those PBMs continue to represent the interests of insurance plans and patients effectively? Or will they have an incentive to favor their parent company's drugs over others?[14] The FDA has begun to regulate the advertising and marketing practices of PBMs owned by pharmaceutical manufacturers.[15] The Federal Trade Commission is also looking into those issues.

Another change in the industry involves the growing proportion of drugs distributed through mail-order pharmacies. Many insurance plans now include an option to purchase drugs by mail. According to IMS America, between 1991 and 1996 the share of prescription drugs channeled through mail-order pharmacies grew from 6 percent to 10 percent of manufacturers' total sales revenues.[16] Mail-order pharmacies are able to obtain substantial discounts on brand-name drugs from manufacturers in part because, in a mail-order setting, pharmacists have more time (about two days) to contact doctors and obtain permission to switch a prescription to a less expensive brand-name drug.[17] In addition, mail-order pharmacies appear to be more effective in promoting generic substitution than retail pharmacies.[18] Also, drugs ordered through a mail-order setting are frequently for chronic conditions, so the savings from switching the prescription

11. See General Accounting Office, *Pharmacy Benefit Managers: Early Results on Ventures with Drug Manufacturers*, GAO/HEHS-96-45 (November 1995), p. 7. That report refers to formularies that charge a higher copayment for nonformulary drugs as "incentive based" formularies. Other insurers, including many HMOs, have a very small copayment difference between brand-name and generic drugs and therefore rely more on their doctors and pharmacists (rather than price) to promote generic substitution; see Levit and others, "National Health Expenditures, 1995," p. 185.

12. Jonathan P. Weiner and others, "Impact of Managed Care on Prescription Drug Use," *Health Affairs* (Spring 1991), p. 145.

13. See Milt Freudenheim, "Pharmaceutical Giant Is Buying Operator of Drug-Benefit Plans," *New York Times*, July 12, 1994, p. A1. For a ranking of PBMs by size in 1994, see Milt Freudenheim, "A Shift of Power in Pharmaceuticals," *New York Times*, May 9, 1994, p. D1.

14. See General Accounting Office, *Pharmacy Benefit Managers: Early Results on Ventures with Drug Manufacturers*.

15. See Bruce Ingersoll, "FDA to Watch Drug Switching, Sales Practices," *Wall Street Journal*, January 16, 1998, p. B1.

16. For the 1991 figures, see "Mail Order Grew 37 Percent to $2.9 Billion in 1991 IMS Survey: Growth May Slow Soon," *The Pink Sheet*, F-D-C Reports, March 16, 1992, p. 11. For the 1996 figures, see Pharmaceutical Research and Manufacturers of America, *1997 Industry Profile* (Washington, D.C.: PhRMA, March 1997), p. 31.

17. For a discussion of how Medco obtains discounts from manufacturers, see Brian O'Reilly, "Medco Containment Services," *Fortune*, February 24, 1992, p. 10. See also Thomas M. Burton, "Eli Lilly's Lack of Success with PCS May Soon Lead to a Major Write-Off," *Wall Street Journal*, June 5, 1997, p. A3.

18. In 1992, Medco dispensed a generic drug on 72 percent of prescriptions for a multiple-source drug; statement of Judith L. Wagner, Office of Technology Assessment, before the Senate Special Committee on Aging, November 16, 1993.

are greater since the drug will be taken for a long period of time.

In addition, links have developed between PBMs and mail-order pharmacies. In 1996, PCS Health Systems, the largest PBM, opened a mail-order pharmacy; and the largest mail-order pharmacy, Medco, also has a PBM business.

In sum, the increasing management of outpatient drug benefits has put downward pressure on prescription drug costs by lowering the average prices that both manufacturers and pharmacists receive for those drugs. The promotion of generic substitution has also been a key factor in holding down the average price of prescription drugs (and is something that is more easily accomplished in a pharmacy setting than favoring one brand-name drug over another).

How Managed Care Affects the Demand for Prescription Drugs

To encourage people to enroll in managed care plans and accept a limited network of providers, such plans typically charge lower copayments for physician visits and other medical services (when the limited network is used) than traditional fee-for-service plans do. Those lower copayments tend to increase the use of physicians' services, which in turn increases the demand for prescription drugs.[19] HMOs generally also have more extensive prescription drug coverage than most fee-for-service plans. According to a 1993 survey by the Bureau of Labor Statistics, HMOs typically charged $3 to $5 for a prescription drug purchase, with no deductible, compared with a 20 percent copayment and a deductible (covering all medical services) in most fee-for-service plans.[20] Those lower prescription costs to the patient may increase the proportion of prescriptions that are actually filled. Indeed, some drug manufacturers believe that HMOs have contributed to the increase in the volume of prescription drug sales.[21]

A study by researchers at RAND suggests that a lower copayment structure for both physician visits and prescription drugs boosts the use of such drugs. The study randomly enrolled people in various fee-for-service plans that differed primarily in their coinsurance rates and deductibles. After adjusting for differences in population characteristics, the authors concluded that annual prescription drug spending per person was one-quarter less in plans with a 25 percent coinsurance rate, no deductible, and a $1,000 cap on out-of-pocket expenditures than in plans in which all medical services were free. When the coinsurance rate was increased to 95 percent, drug spending per person was 43 percent lower than when all services were free.[22] Those results suggest that the smaller copayments and absence of deductibles for prescription drugs and physicians' services that are typical of many managed care plans lead to greater use of prescription drugs.[23]

Moreover, a later study found that more prescriptions were bought per person in several HMOs than in a fee-for-service plan that offered comprehensive prescription drug coverage.[24] The fee-for-service plan, like the HMOs, required only a small copayment for prescription drugs and no deductible. In the three cases in which age adjustment was possible, the

19. See Congressional Budget Office, *Updated Estimates of Medicare's Catastrophic Drug Insurance Program* (October 1989), p. 47, for a discussion of the relationship between physicians' services and prescription drug expenditures.

20. Department of Labor, Bureau of Labor Statistics, *Employee Benefits in Medium and Large Private Establishments, 1993,* Bulletin 2456 (November 1994), p. 44 and Tables 64, 66, 85, and 86. The full results from the bureau's 1995 survey have not yet been published.

21. See Levit and others, "National Health Expenditures, 1995"; and IMS America, "IMS Says Managed Care Drove Unprecedented Growth in Pharmaceuticals in 1996" (press release, April 14, 1997, available at http://www.ims-america.com/communications/pr_growth.html).

22. Arleen Leibowitz, Willard G. Manning, and Joseph P. Newhouse, "The Demand for Prescription Drugs as a Function of Cost-Sharing," *Social Science Medicine*, vol. 21, no. 10 (1985), pp. 1063-1069, Table 4. See also Willard G. Manning and others, "Health Insurance and the Demand for Medical Care: Evidence from a Randomized Experiment," *American Economic Review* (June 1987), pp. 251-277.

23. The results of the RAND study do not indicate whether physician coverage or drug coverage has a greater effect on the quantity of prescriptions sold.

24. Weiner and others, "Impact of Managed Care on Prescription Drug Use," pp. 141-153. The HMO plans in the study did not employ their own doctors, but instead contracted with doctors that also had their own private practice.

HMOs nevertheless had 5 percent to 20 percent more prescriptions dispensed per beneficiary than the fee-for-service plan. That result suggests that the treatment practices of HMOs may favor more intensive use of prescription drugs than the procedures of fee-for-service plans do, perhaps as an alternative to costlier forms of treatment. (However, the study did not mention the copayment structure for physicians' services in the HMOs and fee-for-service plan. If the HMOs had lower copayments for physicians' services, that could partly explain their higher volume of prescription drug use.)

The same study also found that the HMOs used newly approved drugs as much as the fee-for-service plan. They showed no tendency toward a slower diffusion of new innovative drugs. The percentage of prescriptions that were dispensed for a newly approved brand-name drug was the same for the two types of plans. Since the overall quantity dispensed was higher in the HMOs, that implies a slightly higher use of all drugs, including new brand-name ones.

Conclusions

Although some managed care techniques put downward pressure on drug spending by lowering the prices paid for brand-name drugs and promoting generic substitution, other techniques, such as lower copayments for health care services, tend to increase prescription drug use and total drug spending. It is not clear how the increased use of those techniques has affected the net returns from marketing a new drug. PBMs appear to have greater success at negotiating discounts from retail pharmacies than from drug manufacturers (in the form of rebates). Thus, the management of outpatient drug benefits may not have hurt drug companies' returns very much. And the movement of beneficiaries into managed care plans may have had a positive effect on prescription drug use. If managed care has helped increase the use of prescription drugs, which are often less costly than other forms of treatment, then the somewhat lower prices may be at least partially offset by a rise in the quantity of prescription drugs sold.

Those opposing trends (lower prices but higher demand) make it difficult to determine whether total spending on brand-name prescription drugs has increased or decreased because of the rise of managed care techniques—and as important, whether the total profits of those drugs' manufacturers have risen or fallen as a result.

For brand-name drugs still under patent, the effect of managed care on spending could be negligible if the discounts that purchasers obtain are offset by a higher quantity sold. However, since managed care techniques promote generic substitution, their effect on spending and profits is probably negative for brand-name drugs whose patents have expired.

Chapter Three

Pricing and Competition in the Pharmaceutical Market

The federal government has competing policy objectives with respect to the pricing of prescription drugs. On the one hand, it wants to ensure that companies have enough incentive to invest in researching and developing innovative drugs. On the other hand, it wants to discourage them from charging excessively high prices. In general, the government achieves the first goal through a patent system that grants market exclusivity for a limited period of time, allowing companies to recoup their investment in R&D. For the second goal, it relies on competition between similar drugs to hold prices down.

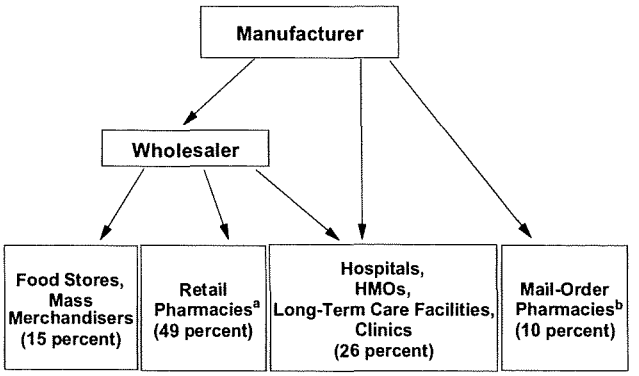
This chapter examines price competition among manufacturers in the pharmaceutical market, including the impact of the dramatic growth in the generic drug industry since 1984. Such competition comes in three main forms: between brand-name drugs in the same therapeutic class, between brand-name drugs and their generic counterparts, and between different generic versions of the same drug. The pharmaceutical industry is also affected by other types of competition, such as the substitution that sometimes occurs between prescription drugs and other forms of medical treatment. However, the conditions under which prescription drugs can be substituted for other medical procedures are outside the scope of this study.

The patent system provides a period of protection during which manufacturers of innovator drugs can charge relatively high prices, earning profits that enable them to compensate for the costs of a drug's discovery and development. Although patents prevent other manufacturers from producing the same drug, they do not prevent manufacturers with a similar but slightly different drug from also obtaining a patent and entering the market. Limited empirical evidence suggests that the availability of several similar brand-name drugs tends to slow the rate of price growth, even before generic copies become available.

The dramatic rise in generic sales since 1984 has held down average prices for drugs that are no longer protected by a patent. However, those lower prices tend not to result from reductions in the price of the original brand-name drug when it begins facing competition from generic drugs. Rather, average prices fall primarily because consumers switch from the higher-priced innovator drug to the lower-priced generics. To be on the receiving end of that switch, generic manufacturers compete with each other intensely in the area of price, partly because they sell identical products.

The increased use of generic drugs has kept total spending on prescription drugs below what it might otherwise have been. Considering only drugs sold through retail pharmacies, the Congressional Budget Office (CBO) estimates that the purchase of generic drugs reduced the cost of prescriptions (at retail prices) by roughly $8 billion to $10 billion in 1994. That estimate assumes that all generic prescriptions dispensed would have been filled with a higher-priced brand-name drug if the generic was not available.

Figure 2.
Channels of Distribution for Prescription Drugs



SOURCE: Congressional Budget Office based on Micky Smith, *Pharmaceutical Marketing Strategy and Cases* (New York: Pharmaceutical Products Press, 1991), Chapter 3; Boston Consulting Group, *The Changing Environment for U.S. Pharmaceuticals* (Boston: Boston Consulting Group, April 1993); and Pharmaceutical Research and Manufacturers of America, *1997 Industry Profile* (Washington, D.C.: PhRMA, March 1997), p. 31.

NOTES: Figures in parentheses represent shares of the prescription drug market in 1996, calculated as a percentage of total U.S. sales at manufacturer prices.

HMOs = health maintenance organizations.

a. Some chain-store pharmacies buy directly from the manufacturer.

b. Some mail-order pharmacies go through a wholesaler.

Much of the analysis in this chapter relies on a set of data that represents 70 percent of prescription drug sales at retail pharmacies in the United States in 1993 and 1994. Roughly half of all prescription drugs are channeled through retail pharmacies (see Figure 2). Thus, the data set represents about 35 percent of all drug sales in the United States in those years. The data include total dollars spent on each dosage form (tablet, capsule, liquid, and so forth) of 454 brand-name drugs, as well as total spending on generic versions of the brand-name drugs whose patents have expired. (For more information about the data, see Appendix A.)

The unit used to measure quantity in the retail pharmacy data is the prescription. That unit can lead to measurement errors, however, since different prescriptions for the same drug come in different sizes. (For example, one prescription may be filled with 30 pills and another with 100 pills.) A statistical bias would occur if more pills were dispensed per prescription, on average, for a generic drug than for its brand-name counterpart. That bias would lead to underestimating the price difference between brand-name and generic drugs. But the bias could run in either direction. Without a better measure of quantity, part of the analysis in this chapter relies on the number of prescriptions to estimate sales volume and to calculate average unit prices. Implicitly, those estimates assume that, in general, prescriptions for a brand-name drug and for its generic equivalent have roughly the same average number of dosage units (such as tablets). All estimates that rely on average prescription prices are based only on tablet and capsule formulations, which constitute 87 percent of sales in the retail pharmacy data set. Those dosage forms yield more reliable average prescription prices.

Competition Among Brand-Name Drugs

In 1994, 83 percent of retail pharmacies' total revenues from selling prescription drugs came from innovator drugs (see Table 1). Those brand-name drugs also accounted for 64 percent of all prescriptions dispensed. Single-source innovator drugs—which, by definition, do not yet face generic competition—made up half of retail pharmacies' revenues from the sale of prescription drugs. Because innovator drugs constitute such a large share of pharmacy sales, the extent to which their manufacturers compete on the basis of price has important implications for consumers.

In general, the higher prices charged for brand-name drugs allow firms to recoup their investment in a drug's discovery and development. Studies have found that, on average, discovering and developing a drug takes 11 to 12 years and costs about $200 million per successful product (in 1990 dollars).[1] That $200 mil-

1. That figure represents the after-tax cost of R&D and was calculated as follows: for drugs developed between 1970 and 1982, manufacturers' out-of-pocket costs were about $100 million per drug, after averaging in the costs of clinical failures. Accounting for the opportunity cost of capital (or the time value of money) nearly triples those costs. But

Table 1.
Market Share and Average Retail Prescription Price, by Type of Drug, 1994

	Market Share		Average Retail Prescription Price (Dollars)
	Percentage of Retail Pharmacy Sales[a]	Percentage of Prescriptions Dispensed	
Innovator Drugs			
Single source	55.5	37.5	53.80
Multiple source[b]	27.2	26.5	37.40
Generic Drugs	17.3	36.0	17.40

SOURCE: Congressional Budget Office based on tabulations of retail pharmacy sales data from Scott-Levin.

a. Calculated at retail prices.

b. If generic versions of an innovator drug were available in any dosage form, then all sales of all dosage forms of the innovator drug were classified as multiple source. Hence, an extended-release dosage form that had no generic versions available was classified as a multiple-source drug if generic versions of the original formulation were available.

lion figure includes the cost of drugs that never make it to market; it also accounts for the cost of capital—that is, the cost of waiting for a return until the drug is introduced. Actual drug development costs may be higher today if, for example, the cost of conducting clinical trials has increased. Conversely, costs may be lower if the failure rate of drugs that go into clinical trials has declined.[2]

The stream of after-tax profits over the life of a typical innovator drug follows an up-and-down pattern (see Figure 3). The first 11 to 12 years show a negative cash flow while the drug is being developed, undergoing testing, and awaiting approval. Over the next 20 years, as the drug is marketed, it earns back a return on the investment in its research and development. According to two studies, that profit stream has an average present value of $220 million to $230 million (in 1990 dollars, after deducting manufacturing, advertising, distribution, and other non-R&D-related costs, discounted to the date of market introduction) —which more than compensates for the $200 million in average capitalized costs of drug development.[3] Those studies estimate that for innovator drugs introduced in the early 1980s, after-tax profits exceeded development costs by $22 million to $36 million, on average (in 1990 dollars, where returns are discounted and costs are capitalized to the date of market introduction). Since the returns from selling new drugs are highly skewed—a few drugs earn very large profits, whereas others may only cover the cost of their own development—that average encompasses both a few big winners and some marginally profitable drugs.

The FDA Approval Process

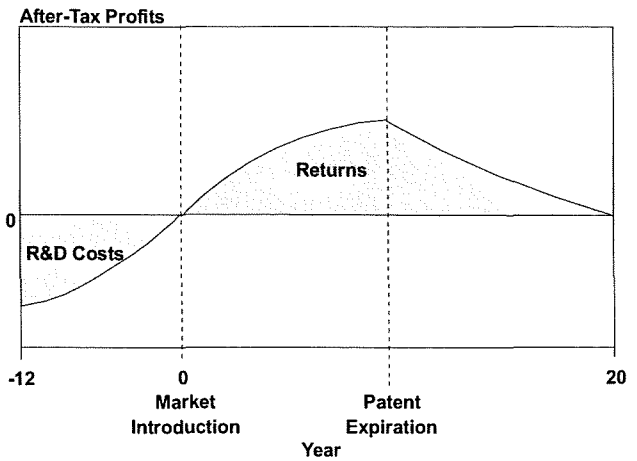
Much of the capitalized cost of drug development can be attributed to the length of the discovery, develop-

since R&D investments are expensed for tax purposes (because a dollar invested in R&D is a dollar on which corporate profit taxes are not paid), the after-tax cost comes to about $200 million at a marginal tax rate of 35 percent. See Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards* (February 1993); and Henry G. Grabowski and John M. Vernon, "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics*, vol. 13, no. 4 (December 1994), pp. 383-406. Both of those studies rely on Joseph A. DiMasi and others, "Cost of Innovation in the Pharmaceutical Industry," *Journal of Health Economics*, vol. 10, no. 2 (July 1991), pp. 107-142.

2. For a discussion about how changes in technology have affected the R&D process, see Geoffrey Carr, "A Survey of the Pharmaceutical Industry," *Economist*, February 21, 1998. As one example, computer programs are being developed that can help predict whether a clinical trial is likely to work before it is undertaken.

3. See Grabowksi and Vernon, "Returns to R&D"; and Office of Technology Assessment, *Pharmaceutical R&D*. Those measures account for the cost of capital, so the returns are beyond the amount necessary to adequately compensate investors for their investment in drug development.

Figure 3.
Change in the Profit Stream for a Typical Innovator Drug



SOURCE: Congressional Budget Office based in part on Henry G. Grabowski and John M. Vernon, "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics*, vol. 13, no. 4 (December 1994).

NOTE: R&D = research and development.

ment, and approval process. That process includes five distinct phases, the first of which is screening and discovery. Recent advances in biomedical research appear to have increased productivity in the discovery phase by yielding new "targets" (such as enzymes) against which a chemical can be tested for interactions. A process called high-throughput screening allows hundreds of chemicals to be tested quickly against a single target. After finding a drug candidate that interacts with the target, the manufacturer checks the drug for toxicity and tests it in animals. If the drug still looks promising, the company files an investigational new drug application with the Food and Drug Administration in order to begin testing the compound in humans. (Testing can begin 30 days after the application is filed.) Between 1980 and 1992, that screening and discovery phase (including preclinical testing) took an average of two to four years.[4]

The clinical trials that follow are divided into three phases. Phase I tests the new compound on fewer than 100 volunteers (usually healthy people) to determine safe dosage levels and toxicity. Phase II tests the drug on 50 to 200 people who have the disease the drug is designed to combat in order to determine both safety and efficacy. Phase III tests the drug on thousands of people to see whether the benefits are statistically significant.[5] The FDA usually requires two controlled clinical trials in humans (Phase III studies) before approving a new drug.[6] Those trials establish effectiveness, optimal dosage forms, and possible side effects. They can also detect adverse reactions at that stage. Companies often consult with the FDA when designing their clinical tests. After a company believes it has gathered sufficient evidence in Phase III testing, it files a new drug application with the Food and Drug Administration.

Making the drug-approval process as quick and efficient as possible without sacrificing standards of safety and efficacy benefits both the public and pharmaceutical manufacturers. Those were the goals of the 1992 Prescription Drug User Fee Act (PDUFA). Meeting those goals is not a simple task, however, since "inevitably there is a trade-off between speed and certainty" about a drug's safety and effectiveness.[7] The PDUFA imposed fees on pharmaceutical manufacturers when they submit a new drug application for FDA approval. In 1997, those fees totaled $205,000 for a full NDA requiring clinical data for approval. Other types of fees paid by firms that filed NDAs include an annual fee on their manufacturing establishments and an annual fee for the drugs they currently have on the market.[8]

4. Joseph A. DiMasi, Mark A. Seibring, and Louis Lasagna, "New Drug Development in the United States from 1963 to 1992," *Clinical Pharmacology and Therapeutics*, vol. 55, no. 6 (June 1994), pp. 609-622.

5. See DiMasi and others, "Cost of Innovation in the Pharmaceutical Industry"; and Blanchard Randall, *Drug Regulation: Historical Overview and Current Reform Proposals*, CRS Report for Congress 95-962 SPR (Congressional Research Service, September 11, 1995), pp. 7-8.

6. David A. Kessler and Karyn I. Feiden, "Faster Evaluation of Vital Drugs," *Scientific American* (March 1995).

7. Ibid., p. 50. For an explanation of the need for a large clinical trial to demonstrate that a drug is as safe as, and more effective than, existing treatments, see F.M. Scherer, *Industry Structure, Strategy, and Public Policy* (New York: Harper Collins College Publishers, 1996), pp. 353-355.

8. Section 736 of the Federal Food, Drug, and Cosmetic Act of 1938, as amended, 21 U.S.C. 379(h).

Table 2.
Average Time from Clinical Testing to Final Approval for an Innovator Drug

Year of FDA Approval	Number of Drugs in Sample	Average Length (Years)		
		Clinical Testing Phase	NDA Approval Phase	Total FDA Approval Time
1984	8	6.6	3.3	9.9
1985	23	5.0	2.8	7.9
1986	13	6.7	2.5	9.2
1987	14	4.5	3.2	7.7
1988	15	4.9	3.1	8.0
1989	17	5.5	3.1	8.7
1990	17	5.3	2.7	8.0
1991	26	5.2	2.7	7.9
1992	18	4.6	3.2	7.8
1993	14	5.2	3.2	8.4
1994	11	6.6	1.9	8.5
1995	10	6.2	2.5	8.7
Total	186	5.4	2.9	8.2

SOURCE: Congressional Budget Office based on data from the Food and Drug Administration and the Patent and Trademark Office.

NOTES: These figures are for drugs that obtained patent extensions under the Hatch-Waxman Act.

FDA = Food and Drug Administration; NDA = new drug application.

The FDA has used those fees to hire more reviewers and accelerate the approval process. The agency reports that it has eliminated the backlog of applications that were awaiting approval and has sped up approval for applications filed since 1992. According to the FDA, drug applications approved between 1991 and 1992 (that included a chemical never before approved) had a median review time of about 22 months. For applications approved in 1994 and 1995, the median review time was down to about 15 months, falling to 12 months in 1996.[9]

By law, however, the FDA is required to approve all new drug applications within 180 days (or a longer period if agreed on with the applicant).[10] In complying with the PDUFA, the FDA has set a target date of one year for all such applications. It reports that at least 95 percent of the 106 new drug applications filed in fiscal year 1995 met that goal.[11]

The total time a drug spends in development, however, does not appear to have changed much. Steering a new drug through clinical testing in humans to final FDA approval took eight to nine years for drugs approved between 1980 and 1992, according to one study.[12] CBO found similar results for 186 drugs approved between 1984 and 1995 that obtained patent extensions under the Hatch-Waxman Act. Those drugs spent an average of 5.4 years in the clinical testing phase (see Table 2). The NDA approval phase took another 2.9 years, on average, bringing the total development time after clinical testing began to 8.2 years. For drugs approved in 1994 and 1995, the

9. See Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, *Center for Drug Evaluation and Research Fact Book, 1997* (May 1997), available at http://www.fda.gov/cder/about.htm. Note that less than half of all new drug applications include a chemical entity never before approved.

10. Federal Food, Drug, and Cosmetic Act of 1938, as amended, 21 U.S.C. 355(c)(1).

11. See Department of Health and Human Services, Food and Drug Administration, *Fourth Annual Performance Report, Prescription Drug User Fee Act of 1992* (December 1, 1996), available at http://www.fda.gov/ope/96pdufa.htm.

12. See DiMasi, Seibring, and Lasagna, "New Drug Development in the United States from 1963 to 1992."

NDA approval phase was shorter than that average but the clinical testing phase was longer. That suggests that faster NDA review times in recent years may have been partially offset by longer clinical testing periods. However, more data are required to assess whether that is indeed the case.

Last year, the Congress passed the Food and Drug Administration Modernization Act of 1997, which made a variety of changes affecting how the FDA regulates food, medical devices, and prescription drugs. Some of those changes could speed up the approval process for innovator drugs. Under the act, the FDA must formulate a plan to reach compliance with the 180-day limit on NDA approvals and other existing time limits.[13] That plan could further reduce the average approval time for a new drug application if the FDA received enough funding to carry it out. (For example, the agency would probably need to hire more staff.)

The 1997 act also attempts to decrease the time needed for conducting clinical tests by encouraging cooperation between the FDA and pharmaceutical companies. For example, once the FDA has approved an investigational new drug application, its officials are required to meet with the applicant (on written request) to agree on the size and design of the clinical studies necessary for final FDA approval.[14]

Faster approval of new drugs increases the returns that those drugs earn. For example, speeding up the FDA approval phase by one year would boost the average profits from marketing a new drug by about $22 million (at a present discounted value in 1990 dollars).[15] That estimate assumes that the approval is accelerated entirely because the FDA reviews applications and test results more quickly, so the timing of outlays in the R&D process does not change. The estimated benefits arise because firms begin earning a profit on their new drug one year earlier. Such a change would nearly double the estimated $22 million to $36 million by which after-tax profits from selling a brand-name drug exceed drug development costs, on average.[16] As a point of comparison, extending the patent on a prescription drug by one year would increase the present discounted value of its returns by substantially less—about $12 million, on average. An additional effect of faster approvals would be increased competition in the pharmaceutical market as new brand-name drugs were introduced more quickly, providing more competition for existing ones.

"Me-Too" Drugs

Although patents prevent other companies from producing exactly the same drug claimed in the patent, they usually do not prevent the introduction of similar but slightly differentiated drugs. In many cases, several different chemical entities can be found that use the same basic mechanism to treat an illness. Since patents are frequently obtained on a specific chemical formulation, not on a therapeutic mechanism, many patented products are "functionally similar."[17] Thus, a breakthrough drug—the first innovator drug to use a particular therapeutic mechanism—may have only one to six years, at most, of pure market exclusivity before a similar patented drug (sometimes called a "me-too" drug) is approved by the FDA. Of 13 therapeutic categories that CBO examined for this study, the first me-too drug entered the market within one year in six cases and within two to six years in another six cases.[18]

13. Food and Drug Administration Modernization Act of 1997, 21 U.S.C. 393.

14. Food and Drug Administration Modernization Act of 1997, 21 U.S.C. 355(b).

15. According to Office of Technology Assessment, *Pharmaceutical R&D*, and Grabowski and Vernon, "Returns to R&D," the average present discounted value of the profit stream from marketing a new drug over its product life is $210 million to $230 million in 1990 dollars. Thus, at an interest rate of 10 percent, adding a year to that product life by speeding up market introduction could raise returns by $21 million to $23 million.

16. Ibid. Those number are also at a present discounted value in 1990 dollars.

17. Z. John Lu and William S. Comanor, *Strategic Pricing of New Pharmaceuticals*, Working Paper 96-1 (Los Angeles: University of California School of Public Health, Research Program in Pharmaceutical Economics and Policy, October 9, 1996), p. 1.

18. The 13 therapeutic classes were H2 antagonists, beta-blockers, ace inhibitors, cholesterol reducers, serotonin reuptake inhibitors (antidepressants), 5-HT3 receptor antagonists (antinauseants), cephalosporins (1st, 2nd, and 3rd generations), growth hormones, calcium channel blockers, loop diuretics, and benzodiazepines (tranquilizers). Those classes were defined by a mechanism of action clearly distinguished in Facts and Comparisons, *Drug Facts and Comparisons* (St. Louis, Mo.: Facts and Comparisons, 1995).

Consider the example of Tagamet, a breakthrough drug in antiulcer therapies that was introduced in 1977. Tagamet was the first drug to relieve ulcers by blocking the histamine 2 (H2) receptors in the lining of the stomach from stimulating acid production by the parietal cells. Such treatment is generally superior to antacids, which only neutralize stomach acid, as well as to anticholinergic drugs, which block acid production but often have more severe side effects.[19] Six years after Tagamet became available, a second H2 antagonist, Zantac, was approved; it eventually became the largest-selling drug in both the United States and the world. By 1989, two additional H2 antagonists, Pepcid and Axid, were available. Thus, four slightly different drugs using the same therapeutic mechanism (blocking the H2 receptor) were all patentable, and the breakthrough drug had only six years of market exclusivity before being challenged by a competitor using a similar compound.

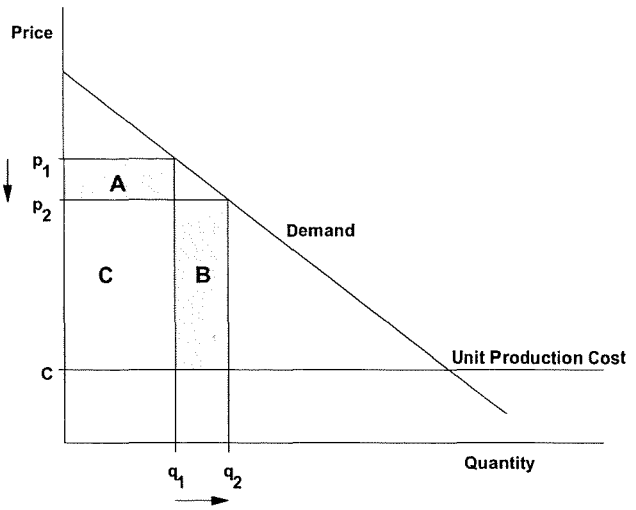
The Economics Behind the Pricing of Innovator Drugs

Although me-too drugs do not offer a novel treatment, they may have fewer side effects and may treat some patients more effectively than the original breakthrough drug. In addition, me-too drugs create more competition in the market by ending the breakthrough drug's monopoly on its method of treatment. That added competition generally keeps the manufacturer of the breakthrough drug from raising its price as quickly as would otherwise be the case.

According to economic theory, both demand and production costs play a role in determining the price of a drug. The line that illustrates demand for a manufacturer's output (known as a demand curve) slopes downward because people will buy more as the price declines (see Figure 4). For example, if the manufacturer's price decreases from p_1 to p_2, then the quantity that the company can sell increases from q_1 to q_2. It is profitable for the manufacturer to lower the price from p_1 to p_2 only if the increase in profits from the larger quantity sold (represented by shaded area B) more than compensates for the loss in profits from the lower price charged on the first q_1 units sold (represented by shaded area A). In this example, the manufacturer would continue to lower the price until it could no longer profit from doing so.[20] The profit-maximizing, or equilibrium, price will exceed the cost of producing another unit of the drug, and the profits earned from selling at that price (represented by areas B plus C, if p_2 is the equilibrium price) provide the incentive for companies to invest in drug development.

When a breakthrough drug is introduced, by definition it has no close substitutes on the market. Demand for the drug is therefore fairly insensitive to

Figure 4.
Choosing a Profit-Maximizing Price for a Drug



SOURCE: Congressional Budget Office.

NOTE: According to this hypothetical demand curve, when the price of a drug declines from p_1 to p_2, the quantity sold increases from q_1 to q_2. Area A represents the loss in profits when the price falls from p_1 to p_2, and area B represents the increase in profits because a greater quantity is sold. Drug companies can increase their profits by lowering price so long as area B is larger than area A. At price p_2, total profits equal area B plus area C.

19. See Ernst Berndt and others, *The Roles of Marketing, Product Quality and Price Competition in the Growth and Composition of the U.S. Anti-Ulcer Drug Industry*, Working Paper No. 4904 (Cambridge, Mass.: National Bureau of Economic Research, October 1994).

20. Economists refer to this as the point at which incremental, or marginal, revenue from selling another unit of the drug is equal to the cost of producing another unit. To keep Figure 4 simple, the cost of producing another unit is assumed to be the same no matter how much is produced (therefore, unit production costs are represented by a horizontal line).

price, since no alternative treatment of equal quality and effectiveness exists. (In other words, the drug has a much steeper demand curve, and a given percentage change in its price is associated with a smaller percentage change in the quantity sold.)

Over time, advertising, "detailing" (visits by representatives of the manufacturer to health care professionals), and articles in medical journals disseminate information to doctors about the new treatment. As the breakthrough drug becomes more widely known, demand for it increases. (Graphically speaking, the demand curve shifts to the right, meaning that at any given price, the manufacturer can sell more of the drug.) At that point, the quantity of the drug sold increases, and its equilibrium price usually rises.

Later, when me-too drugs enter the market, demand for the breakthrough drug becomes more sensitive to price, since close substitutes are now available. At that point, an increase in the price of the breakthrough drug will prompt some purchasers to switch to the substitutes. Advertising and detailing of the new me-too drugs may also cause some customers to switch. Publicity for me-too drugs can also boost demand for the treatment in general. But although the overall market for the treatment may grow, such growth may not offset the sales that the breakthrough drug loses to its new competitors. As the market becomes split among several drugs, demand for the breakthrough drug could shrink and become more sensitive to price. As a result, the price of the breakthrough drug could theoretically decline.

Empirical Evidence About the Pricing of Innovator Drugs

Studies of competition among similar brand-name drugs show that manufacturers compete through prices as well as through advertising and product quality. Most of the empirical studies that look at prices of brand-name drugs are based either on list prices or on average prices paid on invoices to pharmacies and hospitals. Neither of those prices represents an actual transaction price, however. No purchaser pays the list price, although it serves as an important signal since it is a published price observed by all buyers.[21] The average invoice price is much closer to an actual transaction price, but it does not include rebates or discounts that do not appear on the invoice. Since neither price captures the full impact of discounting, studies that rely on those prices underestimate to some extent the level of price competition among brand-name drugs. Those are the only prices widely available to researchers, however, so they are the ones generally used for analyses.

CBO examined the list prices of breakthrough and me-too drugs over time for five therapeutic classes.[22] In four of the five, the list price of the breakthrough product continued to increase in real terms—that is, by more than just the effects of inflation—after the entry of one or more me-too products.[23] In only one case (that of fluoroquinolone anti-infectives) did the breakthrough drug lower its list price in real terms after the first me-too drug entered the market.

A study by John Lu and William Comanor also found that the average list price of brand-name drugs continues to rise faster than inflation after the introduction of a me-too competitor.[24] For 13 drugs that received an A rating from the FDA (as most innovative), the average inflation-adjusted list price after eight years on the market was 7 percent above the launch price. For 48 B-rated drugs (slightly less innovative), the inflation-adjusted list price was 32 percent higher, on average, eight years after launch.

That same study also found that although prices continued to increase, the rate of increase was slower for those drugs that had more brand-name competitors

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21. The list price, called the average wholesale price, or AWP, is published annually in Medical Economics Company, *Red Book* (Montvale, N.J.: Medical Economics Company).

22. Prices were obtained from the 1980 to 1994 editions of the *Red Book*. The five therapeutic classes were H2 antagonists, cholesterol reducers (specifically HMG-CoA reductase inhibitors), antidepressants (specifically serotonin reuptake inhibitors), fluoroquinolone anti-infectives, and alpha-blockers, as listed in Facts and Comparisons, *Drug Facts and Comparisons*.

23. In one of those four cases, the entry price of the me-too drug exceeded that of the breakthrough drug. In the other three, the breakthrough drug's price was not reduced even though the me-too drugs with which it competed were available at a lower price.

24. Lu and Comanor, *Strategic Pricing of New Pharmaceuticals*.

on the market. The introductory price also tended to be lower when more similar brand-name drugs were already on the market. Those findings suggest that the rate of price increase is slowed by competition between brand-name drugs.

A breakthrough drug has an advantage over its me-too competitors in that doctors become experienced with it first and are usually hesitant to try a new drug unless it is seen to be more effective or have fewer side effects. New me-too drugs that offer small advantages over competitors may be sold at a lower price initially; then, as they become more widely accepted, their price rises more quickly.[25] That may partially explain why the list prices of C-rated drugs (least innovative) tend to increase much more rapidly over time than the list prices of their more innovative competitors. Lu and Comanor found that for a sample of 69 C-rated drugs, the average inflation-adjusted list price after eight years on the market was 62 percent above the launch price. That high price increase occurred although those drugs were launched at roughly the same price as their closest competitors, on average.

Price competition among similar innovator drugs is softened because products are differentiated. It is also softened because entry in the pharmaceutical industry is limited by patent protection and the FDA approval process. Still, companies have an incentive to continue to enter the market with similar brand-name drugs until profits are driven down to a normal (competitive) rate of return that adequately compensates for the risk of investing in drug development. One economist has asserted, based on discussions with industry executives, that more me-too drugs are not developed because they would not be profitable given the high development costs.[26] Companies will choose to develop a brand-name drug similar to others on the market only if they believe that the market is not already saturated, or that their drug may have some quality advantage (such as fewer side effects or greater efficacy) that could enable it to compete effectively and earn profits that more than cover the development costs. Competition should result in firms' earning close to a normal rate of return to their R&D investment, on average.

Using average invoice prices, economist Scott Stern found that cross-price elasticities (a measure of buyers' sensitivity to price differences between similar brand-name drugs) in four therapeutic classes were consistent with the assertion that brand-name drugs compete in price.[27] His estimates of price sensitivity were not consistent with the assertion that firms collude to maintain prices as high as what would be charged if a single company produced all of the products. Several other studies have also found that the price differences between patented pharmaceutical products can largely be accounted for by differences in quality, such as side effects and therapeutic effectiveness.[28]

Barriers to Entry and Market Concentration

Competition between brand-name drugs may be limited not only by patent protection but also by the advantages that large drug companies have in marketing and in the FDA approval process. One of the key ways in which firms compete for market share (other than through price) is by advertising. Promotional spending for a brand-name drug can run as high as 20 percent of total sales. In 1989, three-quarters of promotional outlays went toward detailing—financing a large sales force that promoted the firm's entire product line directly to health care professionals.[29] The

25. Economists have analyzed this phenomenon using an "experience goods" or "switching costs" model. See F.M. Scherer and David Ross, *Industrial Market Structure and Economic Performance* (Boston: Houghton Mifflin, 1990), pp. 588-589.

26. Scherer, *Industry Structure, Strategy, and Public Policy*, p. 351.

27. The four classes were gout therapies, nonbarbiturate sedatives, oral diabetic therapies, and minor tranquilizers. See Scott Stern, "Product Demand in Pharmaceutical Markets" (draft, Stanford University, Department of Economics, November 21, 1994; the draft was updated in 1996 at MIT's Sloan School of Management).

28. See, for example, W. Duncan Reekie, "Price and Quality Competition in Drug Markets: Evidence from the United States and the Netherlands," in Robert B. Helms, ed., *Drugs and Health: Economic Issues and Policy Objectives* (Washington, D.C.: American Enterprise Institute, 1981).

29. Richard E. Caves, Michael D. Whinston, and Mark A. Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry," *Brookings Papers on Economic Activity: Microeconomics* (1991), pp. 11-12; and Mark A. Hurwitz and Richard E. Caves, "Persuasion or Information? Promotion and the Share of Brand-Name and Generic Pharmaceuticals," *Journal of Law and Economics*, vol. 31 (October 1988), p. 302.

Table 3.
Percentage of New Drugs Acquired Rather Than Self-Originated by U.S.-Owned Drug Companies

	Investigational New Drug Applications		Approved New Drug Applications (For new chemical entities)	
	Number of Applications Filed	Percentage of Drugs Acquired[a]	Number of Applications Approved	Percentage of Drugs Acquired[a]
1963-1966	326	19	b	b
1967-1970	240	20	b	b
1971-1974	206	19	b	b
1975-1978	160	21	38	29
1979-1982	185	31	47	40
1983-1986	223	26	40	40

SOURCE: Congressional Budget Office based on Joseph DiMasi, Natalie Bryant, and Louis Lasagna, "New Drug Development in the United States from 1963 to 1990," *Clinical Pharmacology and Therapeutics* (November 1991), p. 475.

a. Cases in which the company submitting the application had acquired rather than discovered the drug.

b. Not available.

ability to spread those promotional costs across a large product line is beneficial in that type of marketing, giving big firms an advantage.[30] They also appear to enjoy an advantage in the drug-approval process: the General Accounting Office found that NDAs from the most experienced sponsors were three times more likely to be approved than those from the least experienced sponsors.[31]

Perhaps because of the advantages enjoyed by large firms, many new drugs are marketed by a company that did not discover them.[32] Of all chemical entities that began clinical testing between 1979 and 1986, around 29 percent were acquired by another company rather than self-originated (see Table 3). And of the new chemical entities that were approved for marketing during those years, 40 percent were acquired rather than self-originated.

At first glance, the pharmaceutical industry does not appear to be highly concentrated. The four largest manufacturers of innovative drugs each accounted for only 6 percent to 7 percent of total U.S. pharmaceutical sales in 1994. And the top 10 companies together shared just 56 percent of the market.[33]

When pharmaceutical sales are divided into narrower submarkets, in which products are grouped only with their immediate competitors, much higher concentration becomes apparent. CBO's retail pharmacy data set divides drugs into narrowly defined therapeutic classes. (For more information about how those classes are defined, see Box 3.) The data cover 66 therapeutic classes that together represent about 70 percent of the total retail pharmacy sales revenues in the United States from 1991 to 1994. In just over half of those classes, the top three innovator drugs accounted for 80 percent or more of retail pharmacy sales in their class (see Figure 5).[34] In only nine of the

30. Economists would also say that economies of scope are important. Economies of scope occur when the production or advertising of more than one product lowers the average cost of those expenditures for all products.

31. General Accounting Office, *FDA Drug Approval Review Time Has Decreased in Recent Years*, GAO/PEMD-96-1 (October 1995), p. 5. "Experienced sponsors" submitted nine or more NDAs between 1987 and 1992, whereas "inexperienced sponsors" submitted four or fewer NDAs and had no affiliation with more experienced sponsors.

32. Large firms may also have advantages in financial markets, overcoming problems of adverse selection and moral hazard to obtain funding more easily. And they can more easily fund a drug's development out of their profits from sales.

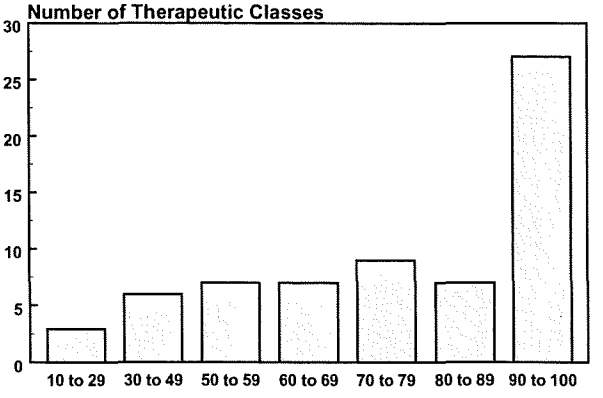
33. Based on U.S. sales reported by *Med Ad News* (September 1995), p. 34.

34. Thirteen of the therapeutic classes contained just one to three innovator drugs. In five of those 13 classes, the top three innovator drugs had less than 63 percent of the market because of generic competition.

classes did the top three innovator drugs make up less than 50 percent of their pharmacy market.

The level of market concentration varies widely among therapeutic classes, however, with concentration reduced by the availability of several different brand-name drugs and by generic entry. Generally, the most concentrated classes in the retail pharmacy data set had four or fewer innovator drugs, none of which were available in generic form. In the 18 least concentrated therapeutic classes, at least one of the three top-selling innovator drugs had a generic version available. And 14 of those 18 least concentrated classes had nine or more innovator drugs.

Figure 5.
Market Share of the Top Three Innovator Drugs in 66 Therapeutic Classes, 1994



SOURCE: Congressional Budget Office based on tabulations of retail pharmacy sales data from Scott-Levin.

NOTE: Market share is calculated as the total sales (valued at retail prices) of the top three innovator drugs in a therapeutic class divided by the total sales of all drugs (both brand-name and generic) in that class.

Box 3.
Defining Therapeutic Classes of Drugs

Drugs are generally assigned to a therapeutic class according to the Uniform Standard of Classification—a system used by many pharmaceutical data companies.[1] Under that system, drugs are grouped by their indication (the type of illness they treat) and their mechanism of action. Each class is assigned a five-digit number. The first two digits represent very broad indications, such as anesthetics, anti-infectives, and cardiovascular therapies. As the number gets larger, the indication becomes more specific—for example, ace inhibitors and beta-blockers are five-digit classes within cardiovascular therapies, and amoxicillin and penicillin fall within anti-infectives.

The degree to which drugs in the same therapeutic class can be substituted for one another varies by class and by drug within each class. In some five-digit classes, the drugs share the same indication but differ in their mechanism of action. For example, all of the drugs in one five-digit class treat ulcers, but some coat the stomach whereas others block acid secretion. In other five-digit classes, each drug has the same mechanism of action (examples are ace inhibitors, beta-blockers, and B-lactamase inhibitors). Prescription drugs that share a five-digit therapeutic class are closer substitutes for one another than drugs in other classes.

1. Both Scott-Levin and IMS America use that system to classify drug sales. The system was developed by IMS America to provide a logical grouping of pharmaceutical products that are considered to compete in the same or similar markets (according to Paul Wilson, Vice President of Statistical Services at IMS America).

Factors That Determine Discounts on Brand-Name Drugs

Different purchasers pay different prices for brand-name prescription drugs. Such discounting, which economists refer to as price discrimination, may be an important mechanism for aiding price competition in the pharmaceutical market.[35] It rewards institutional

35. For a general discussion of price discrimination, see Jean Tirole, *The Theory of Industrial Organization* (Cambridge: MIT Press, 1989), Chapter 3. For a discussion of the legal and economic issues surrounding pricing practices in the pharmaceutical industry, see "Symposium on the Brand Name Prescription Drug Antitrust Litigation," *International Journal of the Economics of Business*, vol. 4, no. 3 (November 1997).

purchasers that organize their patient base through formularies so as to encourage the use of less costly drugs, when possible. Prohibiting or limiting discounts, as some people have called for, could decrease price competition.

A statistical analysis of pharmaceutical prices shows that purchasers tend to obtain higher discounts from manufacturers on brand-name drugs when generic substitutes are available and when a greater number of therapeutically similar brand-name drugs are available. That finding suggests that manufacturers' discounts are a response to competitive market conditions. When a variety of similar drugs are available, the purchaser has more opportunities to switch, which can be used as leverage in negotiating discounts.

The Economic Theory Behind Discounting

If companies practice price discrimination, those purchasers least sensitive to price pay the most. In today's market for outpatient prescription drugs, that means people who have no insurance coverage for drugs, or third-party payers that do not use a formulary to manage their outpatient drug benefits, pay the highest prices for brand-name drugs. Differences in price result because manufacturers apply typical profit-maximizing strategies based on the price sensitivity of buyers. According to economic theory, no purchaser pays a higher price to make up for the discounts offered to somebody else. Instead, each pays the price dictated by his or her price sensitivity.[36]

Manufacturers offer discounts on brand-name drugs based both on the volume bought and on the purchaser's ability to influence market share by systematically favoring one brand-name drug over another. For that reason, one would expect retail pharmacies to pay higher average prices than other purchasers (such as hospitals, long-term care facilities, and health maintenance organizations) because they have less ability to promote such brand-name substitution. (As noted earlier, substituting one therapeutically similar brand-name drug for another requires getting the doctor's consent—something that pharmacists in a hurry do not always have time to do.) If pharmacies do pay higher prices, that may be evidence that some managed care techniques, such as the use of formularies, help other types of purchasers obtain discounts from manufacturers.[37] Pharmaceutical benefit management companies, for example, receive rebates from manufacturers precisely because they apply a formulary to a broad patient base, which a retail pharmacy itself generally cannot do.

Types of Discounts

Manufacturers' discounts on brand-name drugs take a variety of forms. Purchasers that buy directly from manufacturers can simply negotiate a lower purchase price. Three-quarters of prescription drugs are bought indirectly, however, through wholesalers. But that does not prevent the purchaser from obtaining a lower price. Manufacturers frequently pay rebates directly to such purchasers based on the volume of drugs they use over a period of time. A demonstrated ability to switch patients to a particular company's drug, evidenced by an increase in the volume used by a purchaser's patient base, may be rewarded with a higher rebate. Some contracts between PBMs and drug companies have been designed in that manner.[38]

Another important form of discounting involves the wholesaler. Together, manufacturers and wholesalers have developed a computerized system whereby the wholesaler learns of the discounted price negotiated between a manufacturer and a particular purchaser. The wholesaler delivers the drug at the discounted price, informs the manufacturer of the discounted delivery, and then is reimbursed by the manufacturer electronically.[39] Such discounts handled

36. See Tirole, *The Theory of Industrial Organization*, pp. 137-139.

37. For a further discussion of this issue, see Kenneth G. Elzinga and David E. Mills, "The Distribution and Pricing of Prescription Drugs," *International Journal of the Economics of Business*, vol. 4, no. 3 (November 1997), pp. 289-292.

38. See, for example, "PCS Rebates from Pfizer on Seven Products Totaled over $10 Million in First 21 Months of 1994-1998 Contract," *The Pink Sheet*, F-D-C Reports, June 10, 1996, p. 16.

39. For a discussion of that system, see F.M. Scherer, "How U.S. Antitrust Can Go Astray: The Brand Name Prescription Drug Litigation," *International Journal of the Economics of Business*, vol. 4, no. 3 (November 1997), p. 248.

Table 4.
Average Price Differences for Various Types of Purchasers in the Pharmaceutical Market (In percent)

Type of Purchaser	Average Invoice Price Paid for 100 Brand-Name Drugs (As a percentage of the average invoice price to pharmacies) 1993	1994	Market Share by Type of Purchaser in 1994[a]
Retail Pharmacies	100	100	85.6
Hospitals	91	91	4.2
Long-Term Care Facilities	96	95	3.4
Health Maintenance Organizations	80	82	2.7
Federal Facilities	65	58	2.6
Clinics	95	91	1.6

SOURCE: IMS America.

NOTE: These figures are based on the average prices of 100 top-selling brand-name drugs sold primarily through retail pharmacies. The prices do not include manufacturer rebates or other discounts not appearing on the invoice.

a. Calculated as a percentage of total sales revenues for the 100 drugs (valued at invoice prices) after excluding sales to mail-order pharmacies.

through a wholesaler are generally known as charge-backs (although that term is sometimes used to encompass other types of discounts as well).[40]

Empirical Evidence on Discounting

Most discounts are negotiated privately between manufacturers and purchasers and do not become public information. CBO was able to obtain limited information from IMS America about the different prices that different types of purchasers paid for some prescription drugs in 1993 and 1994 (see Table 4). The prices paid by pharmacies can be viewed as a proxy for the final price paid by customers who do not have a managed drug benefit or PBM to negotiate rebates from manufacturers. That limited pricing information suggests that customers of retail pharmacies who do not have such a plan are paying the most for brand-name drugs.

The price comparison is based on the average invoice prices paid by various kinds of purchasers for 100 top-selling drugs sold largely through pharmacies. (Top-selling drugs that were dispensed primarily in an inpatient setting, such as a hospital, were excluded.) About 85 percent of the revenues from sales of those drugs (excluding sales to mail-order pharmacies) came from retail pharmacies; the other 15 percent came from sales to other types of purchasers.

Those other purchasers paid less, on average, than retail pharmacies for the drugs in question. That finding is consistent with the notion that purchasers are rewarded for their ability to influence the prescription choice of a large patient base. For example, hospitals and clinics paid 9 percent less than retail pharmacies in 1994, and HMOs paid 18 percent less. Federal facilities got the biggest discount, over 40 percent, off the average invoice price paid by retail pharmacies.[41]

40. For example, hospitals and hospital buying groups sometimes refer to the rebates paid directly to them by manufacturers for drugs bought through wholesalers as charge-backs, even though the wholesalers have no knowledge of them. See Caves, Whinston, and Hurwitz, "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry," p. 32.

41. Note that the prices paid by federal agencies—such as the Department of Veterans Affairs, the Defense Department, the Indian Health Service, and the Public Health Service, as well as state pharmaceutical assistance programs—are not affected by the best-price provision in the Medicaid rebate program, which discourages discounting. That exclusion was made permanent by the Veterans Health Care Act of 1992. For more information, see Congressional Budget Office, *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*, CBO Paper (January 1996); and General Accounting Office, *Drug Prices: Effects of Opening Federal Supply Schedule for Pharmaceuticals Are Uncertain*, GAO/HEHS-97-60 (June 1997).

That comparison is based on invoice prices only, which do not capture rebates and other types of discounts that do not appear on an invoice.[42] The size of the average price differences between types of purchasers, and perhaps also the relative ranking of the nonpharmacy purchasers, would change if rebates and all forms of discounts were included. But as long as the excluded rebates and discounts were not larger for retail pharmacies than for the other types of purchasers, on average, then the conclusion drawn from Table 4—that customers of pharmacies without a managed drug benefit pay the highest prices for brand-name drugs—would remain correct. Unfortunately, more complete pricing data are not available.

Rebates to PBMs and Medicaid are also not included in Table 4. Such rebates are an important mechanism for lowering the average prices that manufacturers are paid for prescription drugs bought through retail pharmacies. Since the invoice prices paid by pharmacies do not include the rebates that PBMs and Medicaid receive, Table 4 probably overstates the difference between the average prices that manufacturers earn for drugs channeled through retail pharmacies and the average prices they earn for drugs channeled through other types of purchasers.

Statistical Analysis of Discounts

For another perspective on pricing in the pharmaceutical industry, CBO analyzed data on the "best-price discounts" offered by manufacturers of brand-name drugs in 1994. (Manufacturers reported that information to the federal Health Care Financing Administration as part of the Medicaid rebate program.) The best-price discount equals the percentage difference between a manufacturer's best price (the lowest price it offers any private purchaser in the United States) and the average price it charges for drugs distributed to retail pharmacies. The best price encompasses all forms of discounting, whereas the average price to retail pharmacies generally does not include rebates paid to PBMs or Medicaid (although it does include all forms of discounts that manufacturers give directly to pharmacies).[43]

The best-price discount alone is not a perfect measure of discounting, because it is not representative of all discounts. It would be preferable from an analytic standpoint to know more about the distribution of different prices paid for a particular brand-name drug and the quantity sold at each price. Such extensive pricing data are not publicly available, however.

Manufacturers are very careful about giving large best-price discounts (more than 15.1 percent of their average price to pharmacies) because, by law, they must give that same discount on all drugs distributed through retail pharmacies that are purchased by Medicaid beneficiaries.[44] Since Medicaid usually constitutes a larger share of a drug's market than any single private purchaser—13 percent of retail pharmacy sales, on average—such a discount can represent a significant reduction in revenues. The Medicaid rebate program makes it less likely that manufacturers would offer a large best-price discount (over 15.1 percent) to just one private purchaser.[45]

CBO's statistical analysis in fact shows that the Medicaid rebate program, which began in 1991, has discouraged discounting on brand-name drugs. For every increase of 3 percentage points in Medicaid's market share for a particular brand-name drug, the best-price discount falls by 1.3 percentage points. (That result does not apply to prescription drugs used exclusively in an inpatient setting, which are generally not included in Medicaid's rebate program.)

42. Invoice prices generally incorporate discounts granted through a charge-back system with wholesalers.

43. For more detailed information on the calculation of those prices, see the Medicaid rebate agreement signed by manufacturers (available at http://www.hcfa.gov/medicaid/drug8.htm). The calculation of the average price that manufacturers charge for drugs distributed to retail pharmacies includes sales and discounts to mail-order pharmacies.

44. Manufacturers pay at least a flat rebate of 15.1 percent of the average manufacturer price for drugs they distribute through retail pharmacies that are purchased by Medicaid beneficiaries. The rebate percentage is equal to the best-price discount only when that discount exceeds 15.1 percent.

45. See Congressional Budget Office, *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*, pp. 22-25.